# Optimisation of Delivery Efficiency in Prostate Intensity Modulated Radiotherapy Planning

By

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Words cannot express my gratitude I owe to my supervisors, Prof William Rae and Dr Omer Ali for their professional advice and assistance which made this research and thesis possible.

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# Abbreviation List

| | |
|---|---|
| 3D CRT | Three-dimensional Conformal Radiation therapy |
| CI | Conformity Index |
| DTA | Distance to Agreement |
| DVH | Dose Volume Histogram |
| EUD | Equivalent Uniform Dose |
| GH | General High |
| HI | Homogeneity Index |
| ICP | IMRT Combination Plan |
| ICRU | International Commissioning on Radiation Units |
| IGRT | Image Guided Radiation therapy |
| IL | Intensity Level |
| IMRT | Intensity Modulated Radiation Therapy |
| IntHigh | Intermediate High |
| IntLow | Intermediate Low |
| Linac | Linear Accelerator |
| MLC | Multi Leaf Collimators |
| MMUS | Minimum Monitor Units per Segment |
| MSA | Minimum Segment Area |
| MSS | Minimum Segment Size |
| MU | Monitor Unit |
| MV | Mega Voltage |
| NTCP | Normal Tissue Complication Probability |
| OAR | Organ at Risk |
| PDP | Planned Dose Perturbation |
| PSA | Prostate Specific Antigen |
| PTV | Planning Target Volume |
| QA | Quality Assurance |
| QUANTEC | Quantitative Analyses of Normal Tissue Effects in the Clinic |
| SH | Simple High |
| SL | Simple Low |
| SLW | Sliding Window |
| SMART | Synchronized Moving Aperture Radiation Therapy |

| | |
|---|---|
| SNC | Sun Nuclear Corporation |
| SSF | Segment Suppression Factor |
| TCP | Tumour Control Probability |
| TNM Staging | Tumour, Nodes and Metastasis Staging |
| TPS | Treatment Planning System |

# Summary

Evidence that supports dose escalation for prostate cancer is growing and with Intensity Modulated Radiation Therapy (IMRT) higher conformal target doses can be delivered. With more segments and higher monitor units (MU's), target conformity can be improved, however this results in longer delivery times, which makes it difficult to ensure accurate dose delivery, as intra-fractional as well as target movement plays an increasing role. Evidence from the literature indicates that secondary radiation-induced cancer risk is proportional to the beam-on time (thus the MU's). Improvements in IMRT delivery efficiency while maintaining plan quality can be achieved by reducing the complexity of an IMRT plan. This can be done by changing the optimization parameters during the optimization process. Less "complex" prostate IMRT plans will require fewer MU's by using less segments resulting in shorter delivery times and therefore reduced risk of secondary cancers. The goal of this study was to recommend a set of optimization parameter values that will improve the delivery efficiency of prostate IMRT treatment plan while maintaining plan quality.

Fifteen clinical prostate IMRT plans (15 MV), already used for treatment, were re-optimized, using a XiO treatment planning system (TPS). Changes in total MU's and segments were evaluated for changes in some of the optimization parameter values. Eleven optimization parameters (some of them used more than once with different values) were used to generate 15 new IMRT combination plans (ICP's) for each patient for both 6 and 15 MV, resulting in 450 plans being assessed. One parameter was changed at a time while all other variables were kept constant. Plan quality was evaluated in terms of four variables: MU, number of segments, homogeneity index and conformity index while the delivery efficiency was evaluated in terms of delivery time. To our knowledge no time delivery model has been proposed for a Siemens® ARTISTE$^{TM}$ Linear Accelerator (Linac). Using the principles given in the literature we derived such a time delivery model by adding the radio frequency wave component and Multi Leaf Collimator delay time. K-means clustering was then used to analyse the data in terms of the five variables and the top 10 ICP's in 3 patients in terms of a faster more conformal, delivered plan were identified.

To confirm the delivery efficiency and accuracy, the fluences of these top 10 ICP's were measured on a Siemens® ARTISTE$^{TM}$ Linac with the step and shoot method and compared to the treatment planning system's fluences. The evaluation criteria chosen were 3% and 3

mm, distance to agreement. A 3 dimensional dose volume histogram program was used to determine the percentage pass rates on the planned target volumes and the organs at risk.

The optimization parameters such as the minimum MU's per segment, intensity level, minimum segment size and minimum segment area; demonstrated the greatest influence on the total number of segments, while the total MU's was most greatly influenced by the filters and intensity level optimization parameter. Controversy exists regarding which energy should be used, 6 MV or 15 MV, when treating prostate cancer. Both energies were considered here during the optimization process and it was concluded that the optimization parameters are not greatly influenced by the beam energy. However, it was seen that beam arrangement has an influence on optimization parameter behaviour. A limitation of this study is that the beam angle distribution was not investigated.

Thus recommendations could be made in terms of which ICP demonstrated the most improved delivery efficiency of a prostate IMRT treatment plan while maintaining plan quality. The optimisation parameter which was introduced to the optimization process was a General High filter.

Gaining knowledge about the behaviour of the optimization parameters during optimization makes it easier to advise and assist treatment planners preparing complex IMRT plans.

**Keywords**: Prostate treatment, Optimization process, Time delivery model, IMRT, Radiation therapy planning, XiO planning, Cluster analysis, Homogeneity index, Conformity index.

# Opsomming

Volgens die literatuur kan ’n verhoogte dosis vir die behandeling van prostaat kanker voordelig wees. Dit kan bereik word met die Intensiteit Gemoduleerde Stralings Tegniek (IMRT). Met die tegniek is verhoogte gekonformeerde teiken dosisse moontlik, maar dit lei tot vermeerdering van totale monitor eenhede (ME’e) en totale segmente, wat weer langer behandelings tyd tot gevolg het. Met langer behandelings tyd begin pasiënt beweging ’n rol speel en word die akkuraatheid van behandeling beïnvloed. Daar is ook bewyse in die literatuur dat sekondêre geïnduseerde kankers proporsioneel is aan die bundel behandelings tyd of totale ME’e. Indien totale ME’e en segmente verminder kan word vir ’n prostaat behandelings plan, sal dit lei na verkorte behandelings tye en die risiko verlaag vir sekondêre kankers. Dus is dit moontlik om ’n minder gekompliseerde plan te skep maar steeds plan gehalte en doeltreffendheid te behou. Volgens die literatuur is dit moontlik wanneer die optimering parameters verander word gedurende die optimerings proses. Die doel van hierdie studie was om ’n stel optimerings parameters voor te stel wat meer doeltreffend sal wees vir prostaat behandeling, maar nie inboet op plan gehalte nie.

Vyftien prostaat IMRT planne (15 MV), wat reeds behandeling ontvang het, is heroptimeer met ’n XiO beplannings sisteem. Elf optimerings parameters, sommige meer as een keer, was gebruik om 15 nuwe IMRT planne te skep, let wel net een parameter is verander op ’n keer. Dis gedoen vir elke pasiënt en beide energieë (6 MV en 15 MV) gevolg, 450 nuwe planne. Die veranderinge in totale ME en segmente is waargeneem tydens heroptimering. Vier veranderlikes is gekies om plan gehalte te evalueer naamlik; ME, segmente, homogene indeks en gekonformeerde indeks. Terwyl die behandelings doeltreffendheid geevalueer is deur behandelings tyd. Sover ons kennis strek was daar nog geen behandelings tyd model geskep vir ’n Siemens® ARTISTE™ versneller nie. Met die beginsels wat verskaf word in die literatuur is ’n behandelings tyd model geskep. Die radio frekwensie golf komponent en die veelvuldige blaar kollimator se vertraagde tyd is bygevoeg. K-gemiddelde tros analise was gedoen op die vyf veranderlikes vir elke pasiënt. Die top 10 kombinasie IMRT planne wat vinniger en ’n beter gekonformeerde teiken dosis gehad het is geïdentifiseer.

Die tydvloed van die top 10 geïdentifiseerde IMRT planne is gemeet op ’n Siemens® ARTISTE™ versneller en vergelyk met die beplannings stelsel se tydvloed deur ’n 3% en 3 mm kriteria te gebruik. ’n Rekenaar program (3-dimensionele volume histogram) was gebruik

om die tydvloed te analiseer en die dosisse op die teiken orgaan (prostaat) en risiko organe te evalueer.

Die optimerings parameters soos die minimum ME'e per segment, intensiteit vlakke, minimum segment grootte en minimum segment area; het 'n groot invloed gehad op totale segmente. Terwyl die totale ME'e meestal beïnvloed is deur filters en intensiteit vlakke. Daar heers kontroversie oor wat die beste energie is om prostaat kanker te behandel, 6 MV of 15 MV. Beide energieë was gebruik gedurende die optimerings proses en daar is bevind dat die optimerings parameters word nie deur energie beïnvloed nie. Alhoewel, bundel verdeling het wel 'n invloed gehad op die uitkoms van die optimerings parameters. 'n Tekortkoming van hierdie studie was om die invloed wat bundel verspreiding op optimerings parameters het, te ondersoek.

Die beste kombinasie plan is wanneer die algemene hoë filter in gestel was gedurende die optimerings proses, want behandelings doeltreffendheid is verbeter terwyl plan gehalte behoue gebly het.

Gedurende hierdie studie was kennis ook versamel ten opsigte van die optimering parameters se gedrag. Dus sal dit moontlik wees om advies te kan gee aan beplanners ten opsigte van 'n gekompliseerde IMRT plan.

**Sleutelwoorde:** Prostaat behandeling, Optimerings proses, Behandelings tyd model, IMRT, Bestralings beplanning, XiO beplanning, K-gemiddelde tros analise, Homogene indeks, Gekonformeerde indeks.

# Chapter 1

## 1 Introduction

Worldwide prostate cancer is the second most common cancer diagnosed in men. In 2000, the South African Medical Research Council estimated that about 6.1% of cancer deaths among men were caused by prostate cancer[1] and according to the South African National Cancer Registry (NCR)[2], prostate cancer incidence in South Africa is increasing by approximately 3% annually.

Prostate cancer is a slow growing tumour, however if left untreated the cancerous cells can metastasize to other parts of the body. External beam radiation therapy (the use of high energy ionising radiation to kill the cancerous cells), as delivered by a Linear Accelerator (linac), is considered a viable treatment option. Conventional three-dimensional conformal radiation therapy (3D CRT) and Intensity Modulated Radiation Therapy (IMRT) are the two external beam radiation therapy techniques that are currently used by the Equra Health group for treating prostate cancer.

Currently evidence that supports dose escalation for prostate cancer is growing, and with IMRT, higher conformal target doses can be delivered to the treatment volume, while doses to normal tissues are still effectively limited so that the toxicity and side effects are less than that of 3D CRT.[3,4,5] The extent or stage of prostate cancer is an important factor to consider when deciding which treatment option will be most suitable. The staging system used is the TNM staging of the tumour; (Tumour (T), nodes (N) and metastasis (M)) which is determined by the oncologist with additional histological and laboratory information including the Gleason score (biopsy) and PSA level. Patients having locally advance disease, thus T2 and greater staging, will benefit from a dose escalation to more than 76 Gy; this can easily be achieved with the IMRT technique[3,5,6]. The IMRT technique is generally selected for planning the treatment when 15% or more of the local pelvic nodes are involved. Therefore, IMRT is regarded as superior to 3D CRT since the target dose can be escalated and improvement of dose conformity can be achieved, while doses to the bladder, small bowel and rectum, which are considered as organs at risk (OARs), are reduced.[7,8,9,10]

The goal of external radiation therapy is to maximize tumour control probability (TCP) while minimizing normal tissue complication probability (NTCP). This is done by using dose

distributions that conform to the target volume in terms of adequate dose to the tumour and minimum dose to the normal tissue. With 3D CRT, radiation beams are shaped to match the target volume and the beams are of uniform intensity across the field. For the 3D CRT technique, wedges or compensators can be used to change the beam intensity profile to improve conformity to the tumour and reduce normal tissue doses and thus decrease NTCP, while for the IMRT technique, multi-leaf collimators (MLC) are used to shape and modulate the beam intensity profile. For the IMRT technique an inverse planning approach is used and it differs from 3D CRT which uses a forward planning approach, which changes beam parameters to try to achieve an acceptable dose distribution. Inverse planning implies that a desired, or defined dose distribution is given to the planning system which then uses optimisation techniques to attempt to find a suitable plan which complies with certain criteria, within a set of defined constraints on the variable beam parameters. Each beam is divided into beamlets (or segments) with varying radiation intensities to conform to the prescribed dose or clinical goals, as defined by the treating radiation oncologist. For inverse planning a dose-based model is used which usually increases the complexity of treatment plans; meaning that the dose of each beam is expressed as a linear combination of the weights of each beamlet. This makes IMRT a technique that can spare more adjoining normal tissue while conformal doses are delivered. This makes IMRT the more complex, but preferred technique.

The optimization algorithm used for IMRT systematically varies some parameters to optimize an outcome without violating a set of stated constraints. This is called a multi-objective constrained optimization problem, which is optimized to deliver a lethal radiation dose to the tumour cells (target), while limiting the radiation doses to the OARs to safe levels. Due to the increase in total number and complexity of beams and intensities required for IMRT, the total number of segments and the number of monitor units (MU) (which is a measure of the amount of radiation dose delivered by the linac) required to achieve this for the treatment plan can be twice as high as that required for the standard 3D CRT treatment plans. With higher MU's and more segments, dose distribution and target conformity will improve, however this introduces longer delivery times. With longer treatment times it becomes difficult to ensure accurate dose delivery because intra-fractional prostate and patient movement will start to play a role.[11,12]

Intra-fractional movement of a prostate can be tracked by an image guided radiation therapy system (IGRT). This involves the implanting of fiducial markers which tracks the intra-fractional movement of the prostate during treatment.[6,13] Although migration is limited and

stability of fiducial markers is claimed to be reliable,[14] potential complications, such as infection are seen when fiducial markers are placed.[15] Image-guided prostate tracking is only available at a very small number of centres and is not available where resources are limited, due to cost implications of both the equipment and the fact that the treatment process is more time intensive.[16,17] Tong et al. (2015) investigated the prostate movement during treatment with a localization system. They found that the proportion of patients where the prostate shifted by more than 3 mm was 10% by the 5$^{th}$ minute and 20% by the 10$^{th}$ minute; prostate and patient movement thus becomes clinically significant with longer delivery times.[18] Cramer et al. indicated that intra-fractional prostate movement is significant for treatment durations of more than 7-9.5 minutes[19]. Li et al. also established that shortening total treatment time to less than 5 minutes will reduce intra-fractional prostate movement.[20] By decreasing the delivery time of an IMRT treatment plan, the intra-fractional movement can be minimized and accuracy of delivery can be improved. Thus knowing the delivery time before a treatment plan is delivered will be advantageous. None of these authors mentioned the implementation of a strategy for reducing the delivery time by changing any parameters within the optimization process.

Li and Xing et al.[21] created a time delivery model for a Varian linac, which makes it possible to calculate the delivery time of a treatment plan before the plan is actually delivered. Mittaur et al.[22] looked into the time delivery model and created one for an Elekta linac to be able to distinguish between clinical treatment plans. No literature was found in which a time delivery model has been proposed for a Siemens® ARTISTE™ linac. Such a model would be helpful when delivery time needs to be known prior to treatment and could potentially be used as a parameter to assess plan quality.

As previously mentioned with the IMRT technique, the total MU's delivered are substantially greater than when using a 3D CRT technique to treat the same tumour. Moret et al. (2009) looked into the relationship between the risk of induced secondary cancers and use of increased MU's in treating patients. They established that the number of MU's is proportional to the received dose within the volume and proportional to the received neutron dose in the scanned treatment area; making the risk of producing secondary induced cancers proportional to the beam on time (total MU's)[23,24]. Hussein et al (2012)[25] investigated the theoretical risk for secondary induced cancers by comparing 6 and 15 MV and they found that for 6 MV the NTCP for rectum is higher with 0.6% compared to 15 MV. Looking at all organs out-of-field there is an increased risk of developing a secondary induced cancer when 6 MV is used.

Chow et al. measured the surface dose generated for both 6 and 15 MV. They found that surface dose was higher for 6 MV than for 15 MV (the neutron dose generated by 15 MV was not taken into account), when the same total beam numbers were used, however increasing the total beams to 9, a significant decrease in surface dose was seen due to the decrease in total MU's per beam[26]. Less MU's are needed to achieve the same clinical goal, thus the surface dose will increase with lower energies and increased MU's.

Therefore the need arises to improve IMRT delivery efficiency while maintaining plan quality. This can be achieved by reducing the complexity of an IMRT plan by limiting the intensity fluctuations.[27] Less "complex" (less modulation), prostate IMRT plans[28] will generate less MU's by using less segments resulting in shorter delivery times and reduced risk of secondary induced cancers. Efficiency (reduced time) of delivery of the treatment will potentially also be achieved.

Several methods have been proposed to achieve less complex IMRT plans, mainly focusing on the optimization parameters, such as changing the minimum monitor units per segment (MMUS), which restricts segments from having MU values below some fixed minimum value, thus preventing the creation of a large numbers of low dose segments with small or negligible numbers of MU's. Adjusting the minimum segment area (MSA) will put a restriction on small segment sizes which, if not restricted can lead to a large number of small segments being created, thus leading to increased total MU's. Applying adaptive smoothing filters can also be implemented to decrease the number of small segments by smoothing out the fluence.[22,29,30,31,32,33,34,28,35] This has been investigated mostly for the Pinnacle Treatment Planning System (TPS). For this study the CMS XiO TPS, version 4.80, (Elekta, IMPAC Medical Systems Inc. USA) will be used which is the most commonly used TPS in our Institution.

The CMS XiO TPS makes use of a multi-objective optimization algorithm which systematically and simultaneously optimizes an objective function to obtain a desired dose distribution. The variables controlling the different objectives in the function are referred to as optimization parameters. Ehrgott et al. identified three steps within an optimization process to achieve the desired outcome.[36] Firstly the beam angle optimization; meaning the number of beams selected and their directions (beam angles was not changed in this study), secondly the intensity pattern for the different beams and lastly the segmentation sequence delivery. All three of these steps are implemented within the CMS XiO TPS. How efficiently these steps are addressed will influence the outcome of an IMRT plan.

During the second step; which is the intensity pattern creation, it is necessary to transform the multi-objective process into a single objective process, meaning that a specific set of weighting factors is used for each variable or optimization parameter selected.[36] The problem with this method is that the weighting factors have no absolute clinical meaning. Thus the clinically relevant outcome of changing the weight of the variables will only be known after the optimization process. The basic mathematical equation for the optimization process is expressed as a function of the weighted sum of the different variables, as displayed by Eq. 1. This function is then minimised.

$$F(w, x) = \sum_{i=1}^{n} w_i F_i(x) \quad (1)$$

where F = the different variables

w = weight of each variable

During the multi-objective optimization usually only the weights of variables are varied, however Holdsworth et al. investigated the optimization process by varying the penalty variables as well and introducing decision criteria such as Equivalent Uniform Dose (EUD) and mean doses to the OAR. This had a large influence on the selected plan;[37] emphasizing the fact that the impact of changing the weights of variables is only seen after the optimization process.

The CMS XiO TPS uses a two-step approach for IMRT optimization as indicated by Figure 1.1. Firstly initial optimization is carried out and the optimization parameters which can be selected, or for which the value can be changed during this initial optimization, are displayed in Figure 1.2. After initial optimization, the beam segmentation method is chosen as displayed in Figure 1.3. The goal of the segmentation part in the optimization process is to reduce the treatment duration while the intensity pattern is not substantially altered.

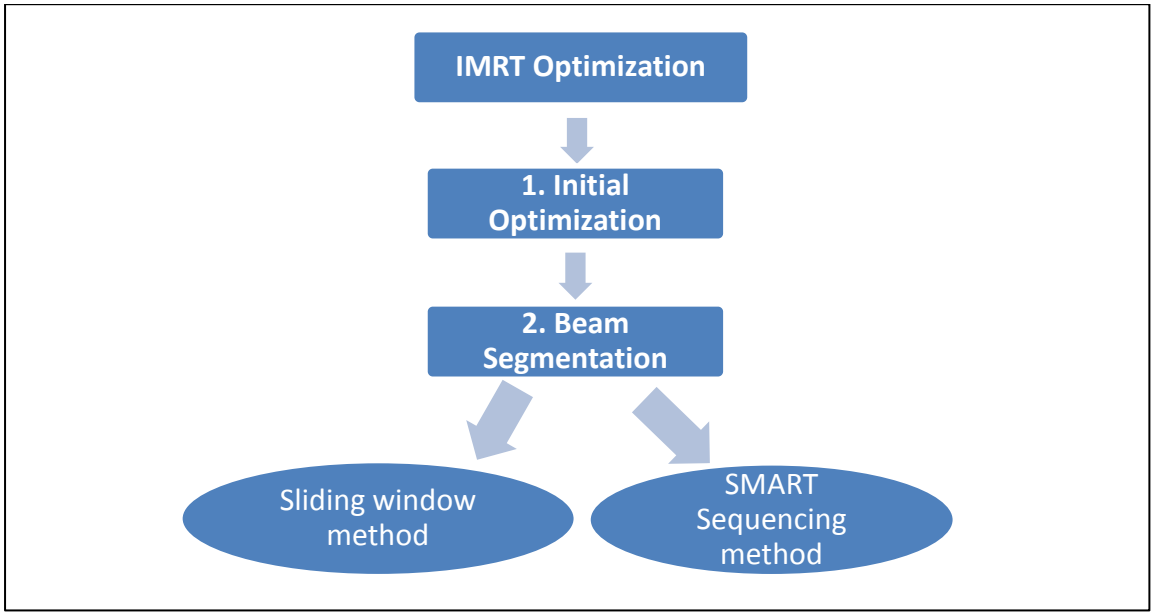



*Figure 1.1: IMRT Optimization is divided into 2 steps, firstly initial optimization is carried out and then the beam segmentation method to be used is chosen.*

The initial optimization parameters, such as the filters, that can be set to control the initial optimization process are shown in Figure 1.2.

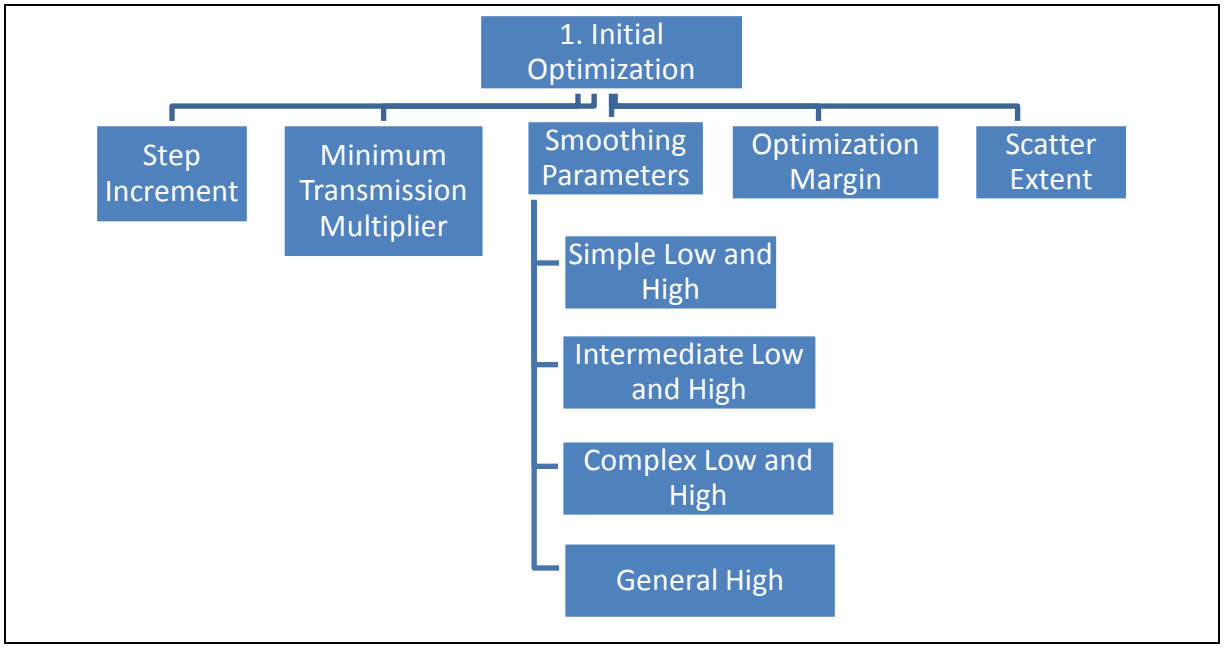



*Figure 1.2: Diagram showing the relationship between the optimization parameters in the XiO TPS that control the initial optimization process.*

XiO uses two segmentation methods as indicated in Figure 1.3; the Sliding Window (SLW) method and the Synchronized Moving Aperture Radiation Therapy (SMART) method. The SLW method generates an arbitrary intensity profile achieved by dynamic jaws or MLC. In

the case of SLW, the MLC sweeps across the field from left to right from the isocentre to deliver the desired profiles (also known as segments), while for the SMART method the TPS generates segments based on clusters or groups of similar intensities, which are delivered by using a step and shoot method of the MLC. Thus when the SLW or SMART techniques are referred to in this document, they refer to the TPS segmentation method and not to any delivery technique available on the linac.

According to the XiO training guide[38] parameters that can be adjusted for the SLW method, include minimum MU per segment (MMUS), Minimum segment size (MSS) and intensity levels (IL). On the other hand the parameters that can be adjusted for SMART sequencing include the minimum MU per segment (MMUS), minimum Segment Area (MSA) and Segment Suppression Factor (SSF), displayed in Figure 1.3.

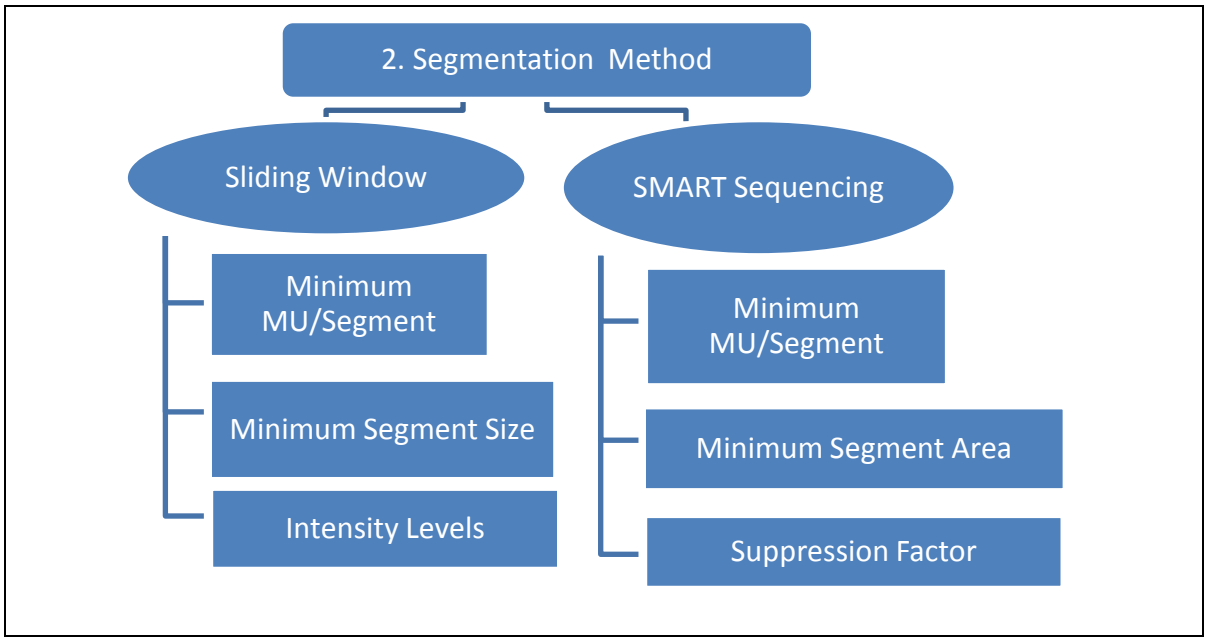



*Figure 1.3: Two segmentation methods are available in the XiO TPS for IMRT optimization, the SLW method and the SMART sequencing method, each controlled by a few adjustable parameters which are listed in this figure.*

According to the literature it appears that the plan quality and MU efficiency are most greatly influenced by the optimization parameters. Mittauer et al. reported that MMUS has a more costly influence on the planning quality and delivery time than the MSA.[22] Qi and Xia reported that even when setting the MSS and MSA to a relatively large value, clinically acceptable IMRT plans could still be generated.[29] Takahashi et al. investigated the influence of MSS on planning quality and dosimetric accuracy. They suggested that the MSS value of 1.5 cm is optimal and should not be larger than 2.2 cm. If the seminal vesicles are added as a

tumour volume the MSS value should not exceed 2 cm otherwise the plan quality will be worsened.[30] They also found that MSS with a value less than 1.5 cm resulted in inaccuracies of dose delivery of more than 5% as determined using Gafchromic film; making small field dosimetry challenging. Matuszak et al. focused on applying an adaptive smoothing filer as a penalty cost function and concluded that it has the least drawbacks in terms of plan degradation.[34]

From the literature it is confirmed that the optimization parameters will have an influence on the plan quality. However plan quality will also be reflected by delivery efficiency; increasing the need to adequately report the delivery efficiency which will be expressed in terms of patient QA results. Improved and revised dose reporting methods are given by the ICRU 83 and will be used in this study for dose reporting.[39] For IMRT dose-volume reporting is generally used because absorbed dose covering the entire Planning Tumour Volume (PTV) can easily be determined from the dose-volume histogram (DVH) and thus controlled through optimization planning. Sun Nuclear Corporation, Melbourne released the 3DVH program in 2010 which allows reporting of the PTV coverage in a 3D manner. Olch et al. established that this method is acceptable and can replace ion chamber and even film dosimetry for patient specific QA[40]. As far as we know, measuring the dosimetric effects of a less "complex" IMRT plan generated by the CMS XiO TPS version 4.80, which is delivered on a Siemens® ARTISTE™ accelerator by the step and shoot method, and then analysing the results in a 3D manner, has not yet been investigated.

There is thus a need to recommend a set of optimization parameter values that will improve the delivery efficiency of a prostate IMRT treatment plan while maintaining plan quality. Plan quality can be evaluated by some function of the total MU's, the number and size of the segments created and the 3DVH program results.[41] This could potentially be achieved by adjusting some of the planning optimization parameters and creating a less complex, more efficient IMRT plan. Delivery efficiency could be evaluated in terms of delivery time, such as the time delivery model of Li and Xing created for a Varian linac.[21] and 2D array measurements. At this stage no such time delivery model has been proposed for a Siemens® ARTISTE™ accelerator. Adjustment of the optimisation process in IMRT planning (control parameters) thus appears to be a promising option towards improving the efficiency of delivery of IMRT to the prostate.

## 1.1 Objective

The objective of this study is to improve the radiation therapy delivery efficiency on a Siemens® ARTISTE$^{TM}$ 160-Leaf accelerator for prostate IMRT by modification of optimization control parameters during the planning process, using a XiO treatment planning system.

# Chapter 2

## 2 Method Overview

Several methods on how to improve plan quality and delivery efficiency for a prostate IMRT plan are mentioned in the literature, as discussed in Chapter 1. According to a preliminary study (Appendix A); changing the set values of the optimization parameters and introducing smoothing filters during the optimization process of an IMRT plan, did result in big changes (up to 50%) for the total MU's and total number of segments. It is therefore natural to ask if these changes in total MU and total number of segments could possibly be utilised to allow improved delivery efficiency of an IMRT prostate plan. In the next few chapters these methods are applied and expanded to determine the most suitable IMRT combination plan (ICP). Figure 2.1 (flow diagram) gives an overview of the methods that will be followed.

The IMRT prostate plans were calculated using the fast superposition algorithm and inverse planning on the CMS XiO TPS version 4.8. A 6 or 7 beam plan, with beams oriented evenly distributed around the patient at 51° intervals was used, as indicated by Figure 2.2. The choice of beam orientation depends upon the tumour size and prescription, which is decided by a planner before planning is started.

Six structures were defined for this study; PTV 1, PTV 2, rectum, bladder, Left and Right femoral heads. All contour volumes and structures were delineated by a radiation oncologist and were used for initial treatment. The PTV sizes of the patients used in this study, ranged from 29 ml up to 1500 ml. The PTV dose prescription[42,43] refers to PTV95 ≥ prescribed dose which varied from 50 – 70 Gy in 2 Gy fractions per day. Doses to the OARs, which were the rectum, bladder, Left and Right femoral heads and small bowel, should meet the requirements of Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) recommendations[44].

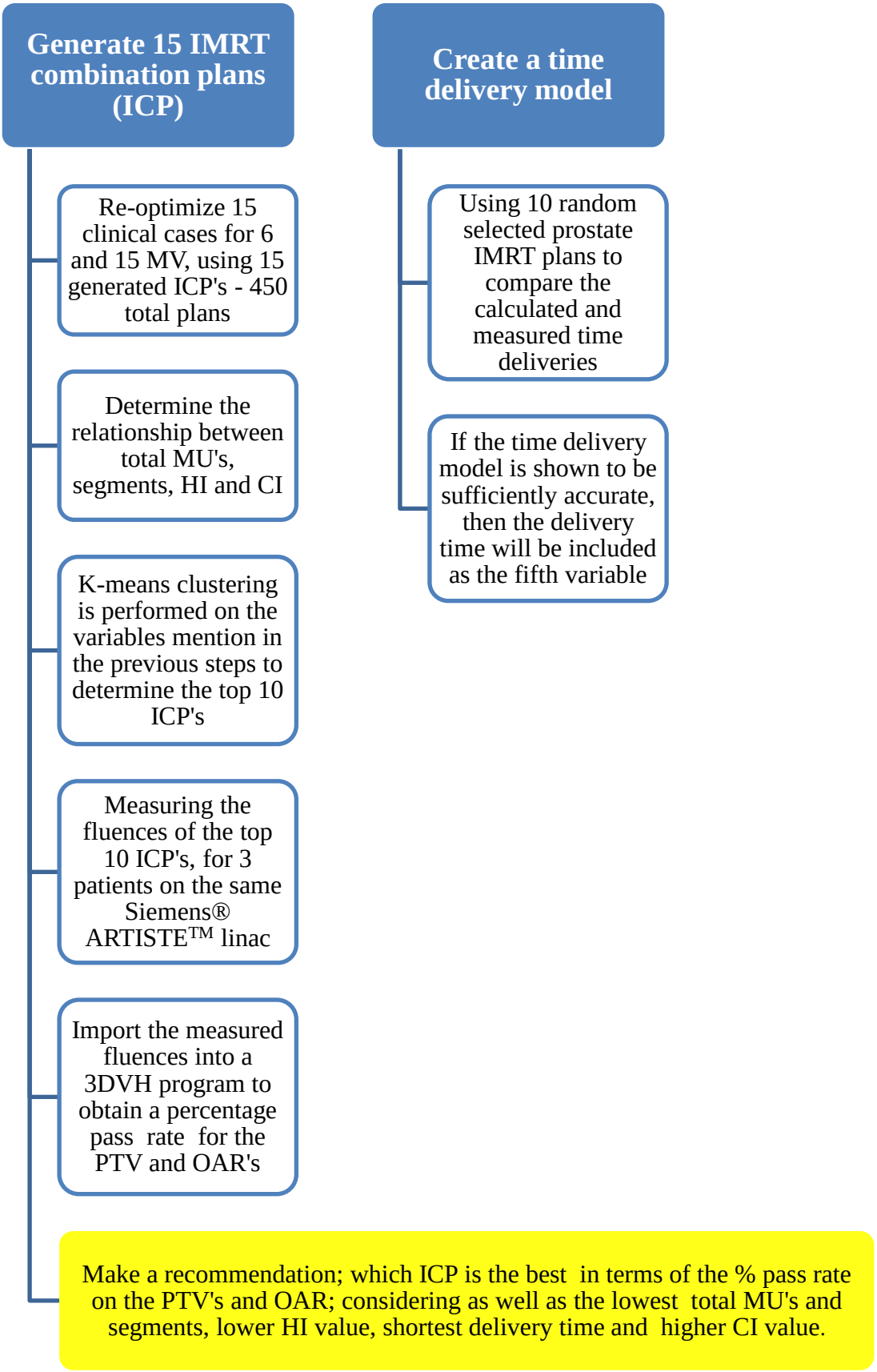



*Figure 2.1: Overview of the methods followed in this study in order to make a recommendation as to which ICP plan is most suitable ("best") for prostate IMRT, and how to obtain such plans.*

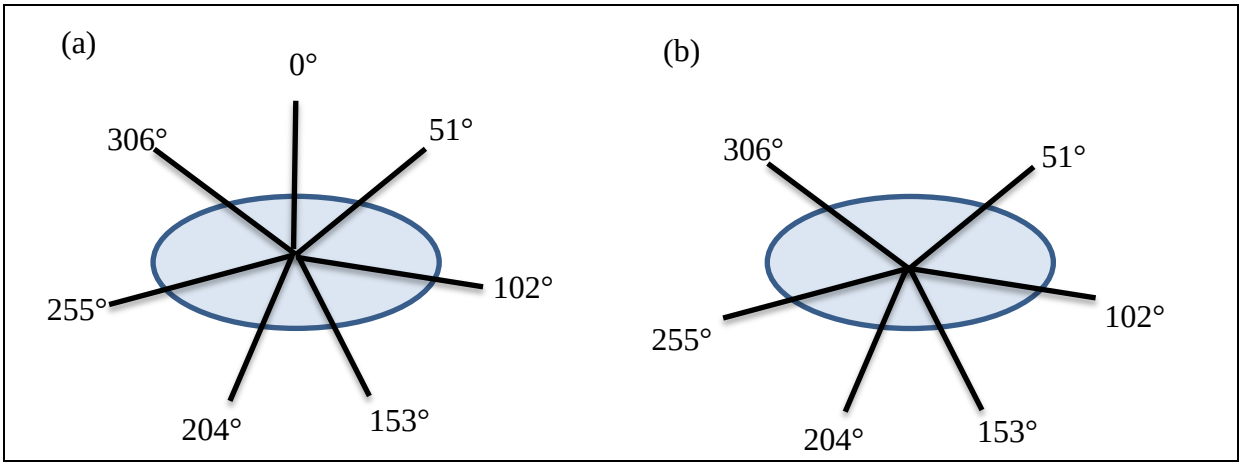



*Figure 2.2: (a): 7 beam orientation with 51° intervals, beam angle start at 0° and end with 306° (b) 6 beam orientation also with 51° intervals, starting at 51° and ending at 306°.*

Chapter 3 describes and expands the method which was followed to re-optimize 15 clinical prostate IMRT plans. Each patient's original plan was re-optimized using 15 different optimization parameter combinations generating 15 new ICP's for each patient; only one parameter was changed at a time (Section 3.2.2). This was done for both energies (6 and 15 MV) resulting in 30 new plans per patient. A total of 450 total new plans were generated.

In Chapter 3, Section 3.2.3, the results of the re-optimized plans are given; the total MU's and total number of segments were noted for each plan, reflecting plan efficiency. Reporting (ICRU 83) of the calculated homogeneity index (HI) and the conformity index (CI) was included for each plan to give an indication of the plan quality[39]. However plan efficiency and quality do not give an indication of delivery time and as mentioned in the literature[12,19,18] referred to in Chapter 1, prostate movement needs to be considered for optimal delivery efficiency.

The delivery times as described in Chapter 4 of all ICP's were calculated, using a time delivery model created for a Siemens® ARTISTE™ 160-leaf accelerator, using the principles given in the literature[20]. The time delivery model in the literature was changed by adding radio frequency (RF) wave warm-up factor and adding the MLC delay component. The calculation of the delivery time for an ICP is given in Appendix C.

The plan quality and delivery efficiency of each ICP as determined in Chapter 3 and 4 could now be evaluated in terms of five variables; MU, segments, homogeneity index (HI), conformity index (CI) and the delivery time. In Chapter 5 k-means clustering was used to analyse the data to determine the top 10 ICP's in terms of a faster more conformal, delivered plan.

Chapter 6 presents the results of the measurements done on the Siemens® ARTISTE$^{TM}$ 160-leaf Artiste linac to confirm delivery efficiency. The top 10 ICP's (determined from chapter 5) generated for 3 patients together with the default plan were measured (three times) using a 2D dosimeter array, called MapCHECK2$^{TM}$ (Sun Nuclear Corporation, Melbourne, Florida). Then the measured dose fluences of the MapCHECK2 together with the TPS dose fluences were imported into a 3D volume histogram (3DVH) (Sun Nuclear Corporation, Melbourne, Florida) program to obtain the delivery efficiency results for the PTV 1, PTV 2 and OAR. With these results a final recommendation was proposed; a set of planning parameters which will improve delivery efficiency while maintaining plan quality.

# Chapter 3

## 3 Re-optimization of IMRT plans

### 3.1 Introduction

#### 3.1.1 Optimization parameters

The implementation of the IMRT optimization technique in a Radiation therapy Department is challenging because prior knowledge of choices regarding the appropriate parameter values, and implications of varying any or all of these parameters, is not always available.

In this chapter the weight of the optimization parameters, also known as variables within the multi-objective algorithm, will be changed to determine if the current "default" settings for a prostate IMRT plan are optimal. As mentioned in chapter 1; the variables' weighting factors have no absolute clinical meaning. Thus the clinical influence of changing the weight of the variables will only be known after the optimization process.

### 3.2 Method

#### 3.2.1 Choosing the optimizing parameters

During a preliminary study (Appendix A) the optimization parameters were varied one at a time to observe their effect on the plan quality. The plan quality was noted in terms of total MU and total number of segments per plan of which an average difference of 12% for the total number of segments and 14% for the total MU's were seen (Appendix A). Eleven optimization parameters showed a difference of more than 10% (felt to be clinically significant)[45] in either the total MU's or total number of segments. They were chosen to be used in this study. Six of these optimization parameters occurred in the Sliding Window method and these were; MMUS, IL's, MSS, general high filter (GH) and the intermediate low (IntLow) and intermediate high (IntHigh) filters. While the other five occurred in the SMART segmentation method as these were; the MMUS, MSA, SSF and the simple low (SL) and simple high (SH) filters. The MMUS, IL and the SSF parameters were used more than once to generate a new ICP selecting a different set value. Thus 11 optimization parameters were investigated generating 15 new IMRT combination plans (ICP).

#### 3.2.2 Generate IMRT combination plans

The chosen optimization parameters, Section 3.2.1 were used to re-optimize 15 clinical IMRT prostate cases that had already finished their treatment. Currently only 15 MV is used

for treatment in our Institution, however 6 MV was also introduced in this study for re-optimization to determine the optimization outcome on beam energy. Thus each patient had 30 new optimized plans (15 x 15 MV and 15 x 6 MV). This resulted in 450 new IMRT combination plans (ICP).

To generate a new ICP the segments of the default plan were deleted. The beam arrangement, energy (initially) and prescription were kept the same. The initial optimization was started after which the segmentation option was selected and the optimization parameter's was changed. We have included an example of the MMUS as indicated by Figure 3.1, all other optimization parameters were changed in the same manner. The optimization process was started again and the re-optimized plan was saved. The total MU's and total number of segments were noted for each plan. After completing all 15 ICP per patient, the process was repeated, changing the energy to 6 MV, however keeping the prescription and beam arrangements the same as per 15 MV.

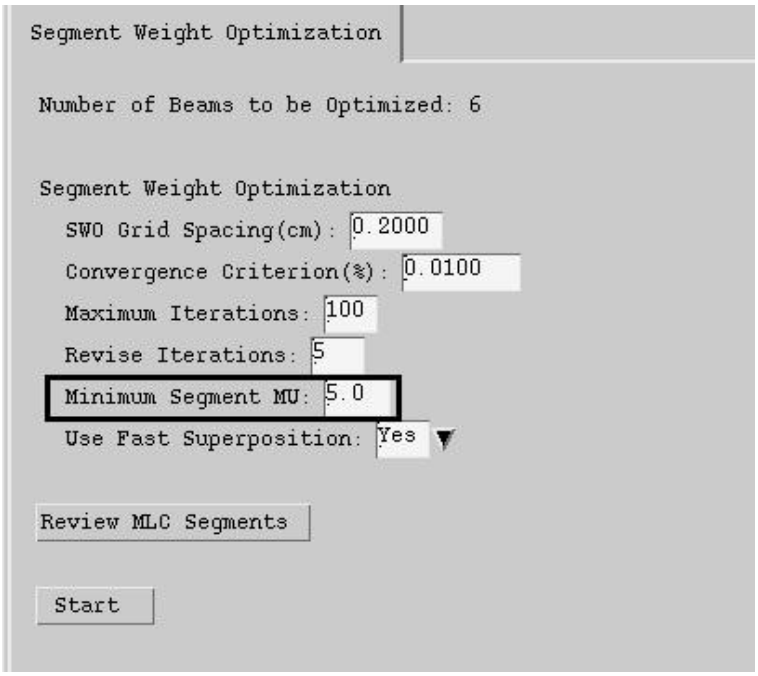



*Figure 3.1: Screenshot of the Segment Weight Optimization tab within the CMS XiO TPS.*

The values of the optimization parameters (Table 3.1) were chosen to be realistic (a value that will most probable be used or currently been used) and then maximum or unrealistic values (most probable not chosen) to indicate the response of each optimization parameter. For example: realistically the linac can deliver 2 MU per segment (plan no. 2) while 8 is the maximum value which can be selected (plan no. 3). An IL of 1 or 2 is unrealistic because the IMRT technique divides the beam into different intensities to spare OAR and conform to the

target. However an IL of 5 or 10 is realistic and 10 is again the maximum value that could be chosen.

For the MSS parameter, 2 is the minimum value and anything above 3 is unrealistic[30] to deliver because the chosen value is squared to create the MSS.[38] The same values ranges were chosen for the MSA parameters as for the MSS, because the segment size and area needs to be small. The SSF combines the segments that have similar sizes and although the range is between 1 - 10, the recommended values are 1-1.5 for a prostate area which has a low gradient region, thus 1, 1.5 and 2 were selected for this parameter as being realistic values.

All these plans were calculated with a 2 mm cubic grid size to achieve the spatial accuracy for dose as recommended by CMS and which is the standard according to the literature.[33,38] All other default values such as the convergence criteria, maximum and revised iterations were kept according to the XiO Training Guide (default settings).[38]

### 3.2.3 Beam quality indexing

Delivering the prescribed dose to a well-defined target; in this case the PTV, while minimizing the dose to the surrounding tissues, requires the dose to conform to the PTV and to be homogeneous within the PTV. To quantify the beam quality of each plan the homogeneity index[46] (HI) and conformity index[47] (CI) were used, calculated as indicated by Equations 2 and 3. Values used for calculating the HI and CI were obtained from the DVH of the TPS.

$$\mathrm{HI} = \left(\frac{D_2 - D_{98}}{D_p}\right) \tag{2}$$

where: $D_2$ is the dose that covers 2% of the target volume

$D_{98}$ is the dose that covers 98% of the target volume.

$D_p$ is the prescribed dose to the target volume.

$$\mathrm{CI} = \frac{\mathrm{TV}}{\mathrm{PTV}} \tag{3}$$

where: TV is the treatment volume receiving 95% of the prescribed dose

PTV is the planning target volume.

A smaller HI value indicates a steeper gradient between $D_2$ and $D_{98}$ dose points, resulting in a more homogeneous dose to the PTV. While a larger CI value indicates that a larger area of the PTV is covered by 95% of the prescribed dose.

## 3.3 Results and Discussion

### 3.3.1 Chosen optimization parameters

Table 3.1 gives an overview of the optimization parameters (underlined) which were chosen to be investigated from the preliminary study. The default plan (Plan no. 1) will be used as the baseline (bold) and at the start of the study the parameters used were comparable with those generally being used to optimize prostate IMRT plans.

*Table 3.1: Optimization parameters (underlined) that were chosen to be investigated for both segmentation methods. Default plan (bold) will be used as the baseline.*

| Plan No. | **SLW** | | | |
|---|---|---|---|---|
| | MMUS | IL | MSS | Filter |
| **Default (1)** | **5** | **7** | **2** | **none** |
| 2 | 2 | 7 | 2 | none |
| 3 | 8 | 7 | 2 | none |
| 4 | 5 | 5 | 2 | none |
| 5 | 5 | 10 | 2 | none |
| 6 | 5 | 7 | 3 | none |
| 7 | 5 | 7 | 2 | GH |
| 8 | 5 | 7 | 2 | IntLow |
| 9 | 5 | 7 | 2 | IntHigh |
| | **SMART** | | | |
| | MMUS | MSA | SSF | Filter |
| 10 | 2 | 2 | 2 | none |
| 11 | 8 | 2 | 2 | none |
| 12 | 5 | 3 | 2 | none |
| 13 | 5 | 2 | 1 | none |
| 14 | 5 | 2 | 1.5 | none |
| 15 | 5 | 2 | 2 | SL |
| 16 | 5 | 2 | 2 | SH |

Note: SLW, sliding window, SMART, synchronized moving aperture radiation therapy, MMUS, minimum monitor units per segment, IL, intensity levels, MSS, minimum segment size, GH, general high, IntLow, intermediate low, IntHigh, intermediate high, MSA, minimum segment area; SSF, segment suppression factor SL simple low, SH simple high.

### 3.3.2 Generated IMRT combination plans

#### 3.3.2.1 All 15 ICP's summarized for both energies

The total MU's and total number of segments were noted for each ICP after optimization for each patient. This is used to investigate what effect each optimization parameter has with respect to the default plan. The percentage difference (difference between the default plan and the new optimized plan) in total MU's for all 15 ICP's, 15 MV are displayed in Figure

3.2. The percentage difference in total number of segments for all 15 ICP's, 15 MV are displayed in Figure 3.3. The maximum (red), minimum (blue) and mean (green) values are indicated on the figures. The black line indicates the variation within that optimization parameter.

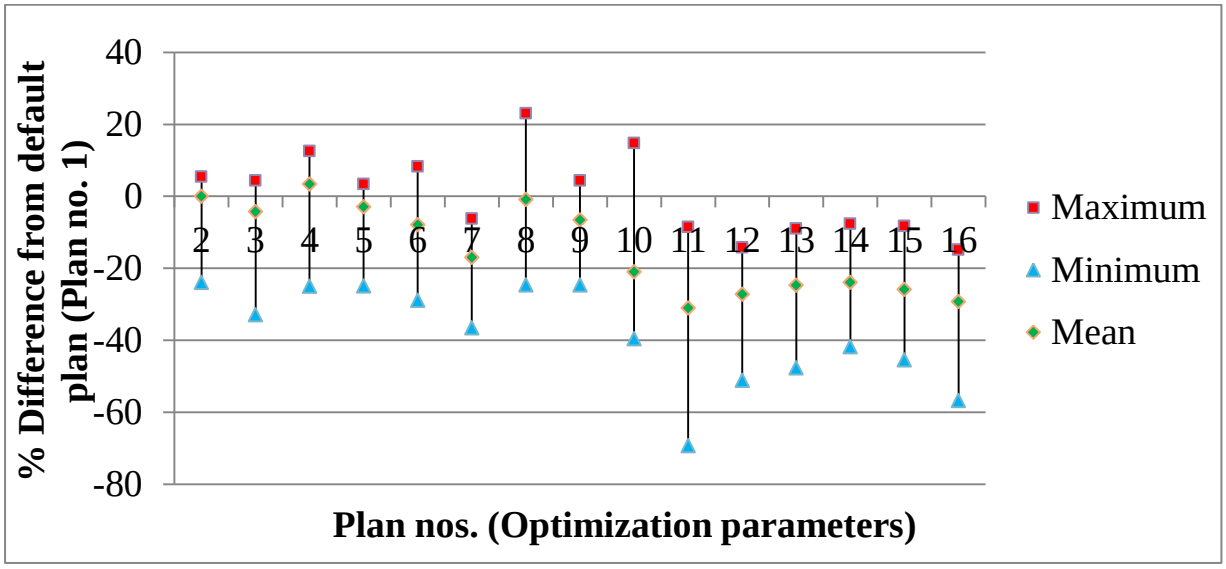



*Figure 3.2: Percentage difference for total MU's of all 15 ICP's compared to the default plan (15MV).*

Plan numbers 2 to 9 were optimized using the SLW segmentation method. Plan no. 7 (General High filter) was the only optimization parameter that did not create more MU's for all 15 patients. Plan no. 4 and 8 created significantly (more than 10%) more MU's (Figure 3.2) which involved the IL set to 5, (Plan no. 4) and adding the IntLow filter, (Plan no. 8).

Plan numbers 10 to 16 were optimized using the SMART segmentation method. The biggest variation in total MU's for all patients was for plan no. 11 (MMUS set to 8). All the plans, except plan no. 10, which involved the MMUS set to 2, created significantly less total MU's (Figure 3.2). Much bigger (up to 95%) percentage differences were seen for the SMART segmentation method. The reason for this can be that the default plan was optimized during the SLW segmentation method.

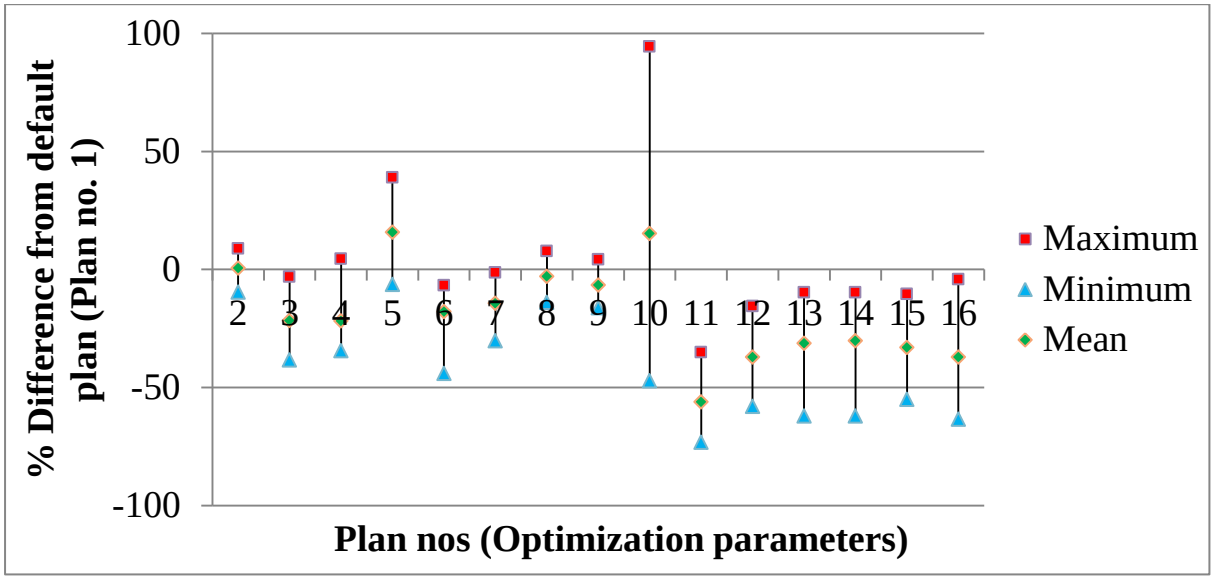



*Figure 3.3: Percentage difference for total number of segments of all 15 ICP's compared to the default plan (15MV)*

Figure 3.3 represents the percentage difference in total number of segments. In plan no. 6 and 7 the total segments was less while for plan number 5 for which IL was set to 10 the total number of segments was significantly more. Thus to reduce the total MU's and total number of segments for an IMRT plan within the SLW segmentation method; the optimization parameters values as given in Table 3.1 for the MMUS, IL and IntLOw filter will not be recommended. In the SMART segmentation part, again all plan nos. created significantly less segments except for plan no. 10 (MMUS set to 2). It seems that the SMART segmentation method is sufficient in creating less segments.

The results of all 15 ICP's optimized for 6 MV are displayed in Figure 3.4 and Figure 3.5.

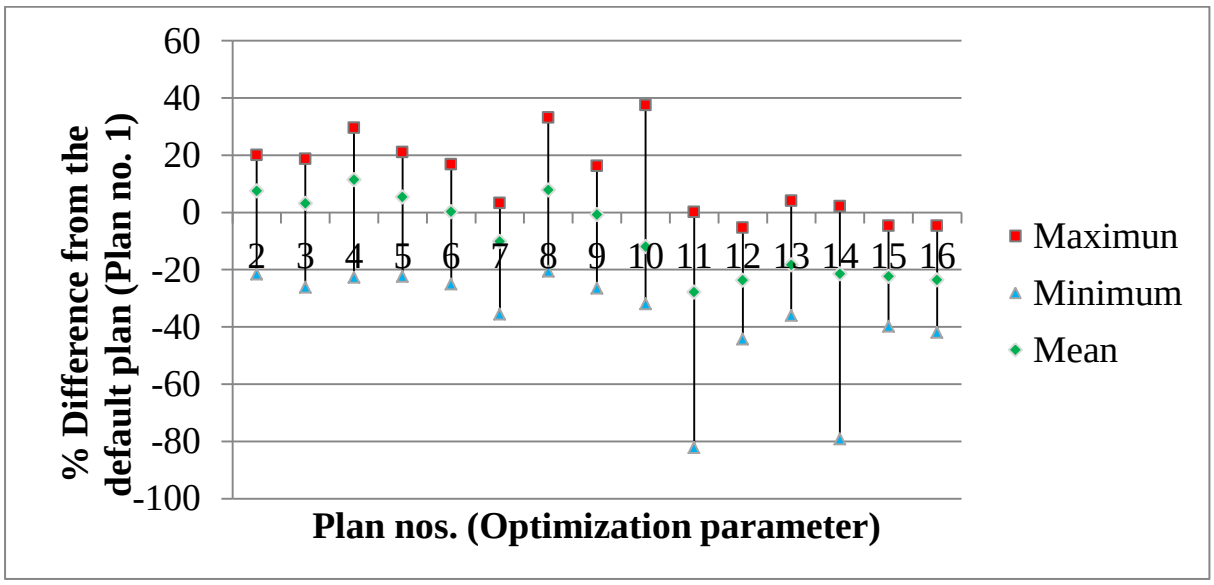



*Figure 3.4: Percentage difference for total MU's of all 15 ICP's compared to the default plan (6 MV).*

Looking at the SLW segmentation method in Figure 3.4 (Plan nos. 2 to 8), most of the time the total MU's increased greatly  except for plan no. 7 (2.2%). In the SMART segmentation part again the biggest variation in data was seen for plan no. 11 (MMUS set to 8). Only plan no. 10 created significantly more MU's.

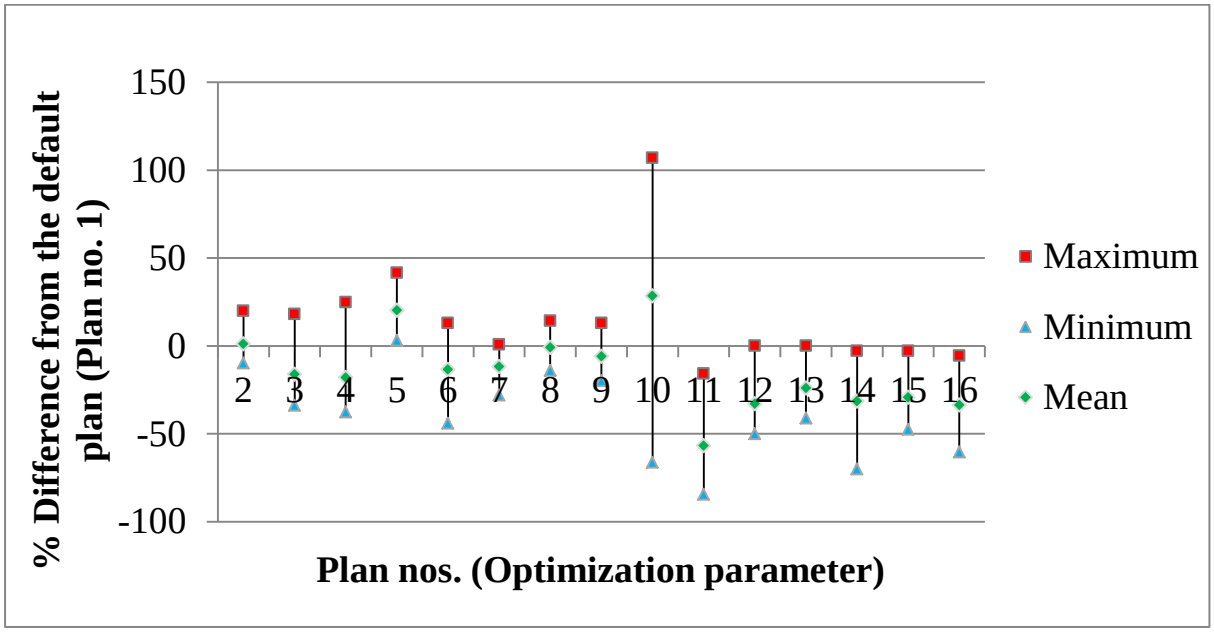



*Figure 3.5: Percentage difference for total number of segments of all 15 ICP's compared to the default plan (6 MV).*

Comparing the total number of segments (Figure 3.5) within 6 MV only in plan no. 7 was the total number of segments decreased for all the patients.  Plan no. 5 showed a significantly increase in total number of segments created, as per 15 MV.

The same scenario was seen for the SMART segmentation method as for 15 MV, all plans except plan no. 10 showed a decreased total number of segments. Plan no. 10 had also the biggest variation for all patients.

The behaviour of the optimization parameters will be discussed in more detail, further in chapter 3. Discussion will involve only one patient, Patient A, unless otherwise stated.

#### 3.3.2.2 Comparing 6 and 15 MV

Table 3.2 contains the results of the 15 re-optimized ICP's for Patient A, 15 MV and Table 3.3 the results for 6 MV. The total MU's was rounded to the nearest integer. The percentage difference for the total MU's and total number of segments was calculated for each new ICP comparing to the default plan (bold). Differences of 10 % and more are indicated in italic font, because it is considered as clinically significant for this study. (Usually clinically significant is seen as ±1 Standard deviation (15 %))[45]

*Table 3.2: Results of the 15 ICP's done for 15 MV for Patient A.*

| PATIENT A – 15 MV | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Plan No. | SLW | | | | | | | |
| | MMUS | IL | MSS | Filter | Total MU's | Total no. of Segments | % Diff MU | % Diff Segments |
| **Default (1)** | **5** | **7** | **2** | **none** | 596 | 68 | | |
| 2 | 2 | 7 | 2 | none | 594 | 74 | -0.3 | 8.8 |
| 3 | 8 | 7 | 2 | none | 585 | 52 | -1.8 | *-23.5* |
| 4 | 5 | 5 | 2 | none | 642 | 57 | *7.7* | *-16.2* |
| 5 | 5 | 10 | 2 | none | 578 | 77 | -3.0 | *13.2* |
| 6 | 5 | 7 | 3 | none | 535 | 54 | *-10.2* | *-20.6* |
| 7 | 5 | 7 | 2 | GH | 478 | 58 | *-19.8* | *-14.7* |
| 8 | 5 | 7 | 2 | IntLow | 579 | 69 | -2.9 | 1.5 |
| 9 | 5 | 7 | 2 | IntHigh | 544 | 63 | -8.7 | -7.4 |
| | **SMART** | | | | | | | |
| | MMUS | MSA | SSF | Filter | Total MU's | Total no. of Segments | % Diff MU | % Diff Segments |
| 10 | 2 | 2 | 2 | none | 420 | 52 | *-29.5* | *-23.5* |
| 11 | 8 | 2 | 2 | none | 545 | 35 | -8.6 | *-48.5* |
| 12 | 5 | 3 | 2 | none | 468 | 44 | *-21.5* | *-35.3* |
| 13 | 5 | 2 | 1 | none | 525 | 55 | *-11.9* | *-19.1* |
| 14 | 5 | 2 | 1.5 | none | 510 | 54 | *-14.4* | *-20.6* |
| 15 | 5 | 2 | 2 | SL | 456 | 47 | *-23.5* | *-30.9* |
| 16 | 5 | 2 | 2 | SH | 479 | 50 | *-19.6* | *-26.5* |

Note: The optimization parameter which was changed each time is underlined. Differences of more than 10% are indicated by italic font. Default plan is highlighted in bold.

In the SLW segmentation method mostly the total number of segments differed more than 10%. Except with plan nos. 6 and 7, for which the total MU's and total number of segments were greatly decreased (more than 10%). Changing the MMUS value from 5 to 2 (plan no. 2) means that the minimum MU in any segment created can be 2 MU's. This results into a less strict criterion, thus allowing the TPS to create more segments. However, changing the MMUS value from 5 to 8 (plan no. 3) meant that any segment should at least have a value of 8 MU. Thus a segment containing a minimum of 7 MU needs be combined in another segment group to have a minimum of 8 MU in total, resulting into a decrease in total number of segments for the plan. The 1.8% decrease in total MU's for MMUS set to 8 (plan no. 3) is expected because less MU's are needed to deliver the same dose; all segments are bigger (segments are joined) thus producing less scattered radiation overall. Mittauer et al. concluded that by increasing the MMUP (Minimum MU per parameter) refers to our MMUS largely impacted the total segments and greatly influence plan quality.[22] Changing the IL value from 7 to 5 (plan no. 4) less intensity are available into which to divide the segments.

This led to a decrease in total number of segments however increasing the total MU's so as to still achieve the desired delivery dose on the PTV. Intensity levels directly influence the number of segments. When the intensity level was changed from 7 to 10 (plan no. 5), the total number of segments increased and a slight decrease in the total MU's was seen.

The MSS parameter caused a large reduction in the total number of segments, -20.6%, which was expected because the segment is deleted if any of the individual apertures in the segment are less than the defined value, which was 3 $cm^2$ (plan no. 6). Takahashi et al. confirmed that large MSS settings largely impacted the total number of segments[30]. If the segments are deleted, the MU's are redistributed among the remaining segments, thus also decreasing the total MU's because segments are bigger and thus less MU's are needed to deliver the desired dose.

The filters, also known as a smoothing function, will be affected by the number of iterations and have a different effect. Less smoothing will be applied to homogenous plans. The general high (GH) filter (plan no. 7) has the highest degree of smoothing, as seen in Table 3.2 among the plans using the SLW method. It was interesting to note that this filter reduces the total MU's more than the number of segments. This is due to the fact that the smoothing function is applied to the intensity fluence before the segmentation is done (during the initial optimisation). The GH filter has a high degree of smoothing; creating fewer segments with higher dose intensities and therefore can leave the OAR more at risk of receiving high doses. The intermediate Low and High filters (plan nos. 8 and 9) are more for general use and the degree of smoothing is not that aggressive, as is seen in Table 3.2 the percentage differences were below 10% for total MU's and total number of segments. The intermediate filters were also more costly on the total MU's than on the total number of segments. Although the filters greatly influenced the total MU's and total number of segments, Matuszak et al. mentioned that smoothing filters have the fewest drawbacks in terms of plan quality when introduced as a cost function.[34]

In the SLW segmentation method, changing the optimization parameter values such as in plan nos. 3, 6 and 7 (MMUS, MSS and GH filter) showed the most promising results for decreasing the total MU's and total number of segments.

Using the SMART segmentation method the biggest differences were seen because both the total MU's and total number of segments differ more than 10%. This can be expected due to the different approaches to optimization between these two methods. SMART segmentation,

also known as the cluster based segmentation method, arranges segments together that have the same dose intensities. For a prostate area which is known as a low gradient area, bigger segments will be created joining the same dose intensities and thus decreasing the total number of segments and MU's.

Changing the optimization parameter value from 2 to 3 for MSA had the second biggest effect of -21.5% on total MU's and second biggest effect of -35.3% on total number of segments of all 15 ICP's this is confirmed by Mittauer et al.[22] This means that all apertures within a total segment area were required to be bigger than 3 $cm^2$ unlike for the SLW method for which it is the requirement is a minimum area for any segment as a whole. The SSF reduces segments by combining segments that have similar sizes; once again a reduction of about 20% in the total number of segments was seen. For a smoothing function the simple low and simple high filters were used, both greatly decreased the total MU's and total number of segments. The degree of smoothing is higher than for the intermediate filters.

Table 3.3 contains the optimization results for 6 MV noted from the TPS. The same patient (Patient A) as for 15 MV was optimized. Thus the only difference between Table 3.2 and Table 3.3 is the energy. The default plan is still the original 15 MV plan which was used to treat the patient. Again a difference of more than 10% is indicated by italic font.

*Table 3.3: Results on the 15 ICP's done for 6 MV for Patient A.*

| PATIENT A – 6 MV | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Plan No. | SLW | | | | | | | |
| | MMUS | IL | MSS | Filter | Total MU's | Total no. of Segments | % Diff MU | % Diff Segments |
| **Default (1)** | **5** | **7** | **2** | **none** | 596 | 68 | | |
| 2 | 2 | 7 | 2 | none | 678 | 75 | *13.76* | *10.29* |
| 3 | 8 | 7 | 2 | none | 679 | 54 | *13.93* | *-20.59* |
| 4 | 5 | 5 | 2 | none | 713 | 57 | *19.63* | *-16.18* |
| 5 | 5 | 10 | 2 | none | 650 | 84 | 9.06 | *23.53* |
| 6 | 5 | 7 | 3 | none | 630 | 61 | 5.70 | *-10.29* |
| 7 | 5 | 7 | 2 | GH | 549 | 60 | -7.89 | *-11.76* |
| 8 | 5 | 7 | 2 | IntLow | 653 | 69 | 9.56 | 1.47 |
| 9 | 5 | 7 | 2 | IntHigh | 643 | 64 | 7.89 | -5.88 |
| | SMART | | | | | | | |
| | MMUS | MSA | SSF | Filter | Total MU's | Total no. of Segments | % Diff MU | % Diff Segments |
| 10 | 2 | 2 | 2 | none | 597 | 34 | 0.17 | *-50.00* |
| 11 | 8 | 2 | 2 | none | 500 | 51 | *-16.11* | *-25.00* |
| 12 | 5 | 3 | 2 | none | 543 | 59 | -8.89 | *-13.24* |
| 13 | 5 | 2 | 1 | none | 543 | 58 | -8.89 | *-14.71* |
| 14 | 5 | 2 | 1.5 | none | 524 | 55 | *-12.08* | *-19.12* |
| 15 | 5 | 2 | 2 | SL | 509 | 51 | *-14.60* | *-25.00* |
| 16 | 5 | 2 | 2 | SH | 487 | 62 | *-18.29* | -8.82 |

Note: The optimization parameter which was changed each time is underlined. Differences of more than 10% are indicated by italic font. Default plan is highlighted in bold.

In the SLW segmentation method, again the total number of segments was mostly decreased as seen with 15 MV. However comparing the values of the two energies in the SLW segmentation method the total MU's were in most cases higher for 6 MV (Table 3.3), indicating that more dose, is needed to deliver the prescribed dose. This is to be expected as the $D_{max}$ for 6 MV (1.6 cm) when compared to 15 MV (3 cm) is at a shallower depth. To correct for this, more beams could be added when using 6 MV before the optimization process begins; however for this study the focus is on the optimization parameters. Ehrgott et el. mentioned that beam angle optimization is the first step for "ideal optimization"[36] and that it is important to approach different anatomical sites differently. However from these results (Table 3.2 and Table 3.3) it seems that beam energy also needs to be addressed differently in terms of beam angles, even when used for the same anatomical site.

Looking at the effect within the SMART segmentation method the total MU's and total number of segments were decreased, as seen with 15 MV, except for the total MU's when

MMUS had a value of 2. The optimization parameters using this segmentation method greatly influences the total MU's and total number of segments, as seen in Table 3.2.

However it is still important to remember that the default plan was optimized during the SLW method which is also the major reason for the large percentage differences found. Looking at the results of Table 3.2 and Table 3.3; the same trend was seen regarding the optimization parameters for both energies, thus the influence on the parameters during the optimization process did not appear to be energy dependent.

#### 3.3.2.3 Comparing beam arrangements

The next step was to determine how the beam arrangements influence the optimization parameters. Table 3.4 contains the results of two patients one having a 6-beam (Patient B) and another 7-beam (Patient A) arrangement for 15 MV. Again the percentage differences are calculated from the default plan and the percentage differences of more than 10% are indicated by italic font.

*Table 3.4: Optimization results expressed in terms of total MU's and total number of segments for two patients, one having a 6 and another 7 beam arrangement.*

| Beam Arrangement | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | **7 Beams** | | **6 Beams** | |
| **SLW** | | | | | | | | |
| | | | | | % Difference | | | |
| Plan No. | MMUS | IL | MSS | Filter | MU | Seg | MU | Seg |
| 2 | 2 | 7 | 2 | NA | -0.3 | 8.8 | 3.03 | 2.22 |
| 3 | 8 | 7 | 2 | NA | -1.8 | *-23.5* | 3.22 | -5.56 |
| 4 | 5 | 5 | 2 | NA | 7.7 | *-16.2* | *10.17* | *-20.00* |
| 5 | 5 | 10 | 2 | NA | -3.0 | *13.2* | -1.90 | *28.89* |
| 6 | 5 | 7 | 3 | NA | *-10.2* | *-20.6* | -8.54 | *-18.89* |
| 7 | 5 | 7 | 2 | GH | *-19.8* | *-14.7* | *-23.88* | *-13.33* |
| 8 | 5 | 7 | 2 | IntLow | -2.9 | 1.5 | *-11.48* | -3.33 |
| 9 | 5 | 7 | 2 | IntHigh | -8.7 | -7.4 | -6.73 | -5.56 |
| **SMART** | | | | | | | | |
| | | | | | % Difference | | | |
| Plan No. | MMUS | MSA | SSF | Filter | MU | Seg | MU | Seg |
| 10 | 2 | 2 | 2 | NA | *-29.5* | *-23.5* | *-20.34* | *94.44* |
| 11 | 8 | 2 | 2 | NA | -8.6 | *-48.5* | *-26.10* | *-46.67* |
| 12 | 5 | 3 | 2 | NA | *-21.5* | *-35.3* | *-26.49* | *-17.78* |
| 13 | 5 | 2 | 1 | NA | *-11.9* | *-19.1* | *-24.38* | *-13.33* |
| 14 | 5 | 2 | 1.5 | NA | *-14.4* | *-20.6* | *-24.38* | *-13.33* |
| 15 | 5 | 2 | 2 | SL | *-23.5* | *-30.9* | *-30.27* | *-22.22* |
| 16 | 5 | 2 | 2 | SH | *-19.6* | *-26.5* | *-26.03* | *-11.11* |

Note: The optimization parameter which was changed is underlined. Differences of more than 10% are indicated by italic font.

From the results in Table 3.4 it is seen that most of the time the optimization parameter behaviour is the same with different beam arrangements, except for the MMUS. In the SLW segmentation method the total MU's decreased for the 7-beam arrangement while it increased for the 6-beam arrangement. Reason for this; when 6-beams are used, more MU's are needed to conform the prescribed dose, while the 7-beam arrangement cover the PTV easier using more angles. This is confirmed by Lim et al. more treatment beams improve plan quality[48]. The same response was seen for most optimization parameters, except with beam arrangement than the optimization approach was different.[36]

#### 3.3.2.4 Comparing different prescriptions

The next characteristic was to see if different prescriptions (50, 60 and 70 Gy) influenced the optimization parameters differently; results are tabulated in Table 3.5.

*Table 3.5: Optimization results (percentage differences) expressed in terms of total MU's and total number of segments of three patients having different prescriptions (50, 60 and 70 Gy).*

| **Prescription** | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | **50 Gy** | | **60 Gy** | | **70 Gy** | |
| **SLW** | | | | | | | | | | |
| | | | | | % Difference | | | | | |
| Plan No. | MMUS | IL | MSS | Filter | MU | Seg | MU | Seg | MU | Seg |
| 2 | 2 | 7 | 2 | NA | 3.91 | 2.35 | -2.24 | 0.00 | 3.70 | 3.08 |
| 3 | 8 | 7 | 2 | NA | 3.03 | *-20.00* | -3.10 | *-27.78* | 0.35 | *-30.77* |
| 4 | 5 | 5 | 2 | NA | 8.89 | *-23.53* | -0.39 | *-30.56* | *10.95* | *-20.00* |
| 5 | 5 | 10 | 2 | NA | 1.79 | *20.00* | -7.54 | 5.56 | -0.17 | *13.85* |
| 6 | 5 | 7 | 3 | NA | -3.72 | *-17.65* | -8.04 | *-15.28* | -5.83 | *-21.54* |
| 7 | 5 | 7 | 2 | GH | -8.14 | -4.71 | *-16.64* | *-15.28* | *-18.12* | *-20.00* |
| 8 | 5 | 7 | 2 | IntLow | 9.24 | 2.35 | -2.39 | -6.94 | -2.30 | -4.62 |
| 9 | 5 | 7 | 2 | IntHigh | -1.66 | -3.53 | -8.03 | -9.72 | *-12.06* | *-10.77* |
| **SMART** | | | | | | | | | | |
| | | | | | % Difference | | | | | |
| Plan No. | MMUS | MSA | SSF | Filter | MU | Seg | MU | Seg | MU | Seg |
| 10 | 2 | 2 | 2 | NA | *-16.48* | *54.12* | *-15.26* | *33.33* | *-23.38* | *-29.85* |
| 11 | 8 | 2 | 2 | NA | *-29.64* | *-61.18* | *-34.48* | *-63.89* | *-24.46* | *-67.16* |
| 12 | 5 | 3 | 2 | NA | *-23.05* | *-37.65* | *-25.48* | *-38.89* | *-19.23* | *-52.24* |
| 13 | 5 | 2 | 1 | NA | *-21.76* | *-37.65* | *-21.34* | *-33.33* | *-17.56* | *-43.28* |
| 14 | 5 | 2 | 1.5 | NA | *-21.76* | *-37.65* | *-21.34* | *-33.33* | *-17.56* | *-43.28* |
| 15 | 5 | 2 | 2 | SL | *-16.96* | *-27.06* | *-19.49* | *-27.78* | *-24.98* | *-47.76* |
| 16 | 5 | 2 | 2 | SH | *-22.89* | *-34.12* | *-23.95* | *-40.28* | *-31.83* | *-53.73* |

Note: The optimization parameter which was changed is underlined. Differences of more than 10% are indicated by italic font.

Comparing the MMUS optimization parameter in the SLW segmentation method it was interesting to see that for the 60 Gy prescription the total MU's and total number of segments were decreased each time with a MMUS value set as 2 and 8, while for 50 Gy and 70 Gy the MU's were increased each time. Almost the same scenario is seen for the IL optimization parameter. The reason for this can be that the 60 Gy total prescription plan had a different beam arrangement (6-beam arrangement) as well. To confirm this; patients with the same beam arrangement and different prescriptions will need to be considered. The GH and IntHigh filters influenced 50 Gy total prescription the least and 70 Gy the most. The same scenario is seen with the SL and SH filters within the SMART segmentation method. An

effective way to decrease the total MU's and total number of segments during optimization for total dose prescription is to use any of the filters, expect the IntLow filter.[34]

### 3.3.3 Closing discussion on the optimization parameters

The optimization parameters such as the MMUS, IL, MSS and MSA mostly influenced the total number of segments of a treatment plan, thus deteriorates plan quality. Mittauer et al. confirmed this by reporting that plan quality degrades with increased MMUS and MSAP values[22]. Having less segments for a treatment plan will improve delivery efficiency resulting in a faster deliverable plan. Patient QA of IMRT plans mostly fails due to the MLC's which cannot form the small segments or cannot deliver segments with low MU's.

Introducing a smoothing filter or if the IL value is increased, the total MU's will decrease as mentioned by Matuszak et al[28], which was also seen in our results. More MU's can increase the risk of secondary cancers thus introducing a filter into the optimization process will be advantageous.

It was unexpected to note that the same behaviour was seen for the optimization parameters when beam energy was changed. Thus it seems the outcome of this study can in future be implemented for beam energies available in the range of about 6 – 15 MV if the same beam arrangement is used because beam arrangement does influence the optimization outcome. It is important to remember that although more beams will provide better conformity to the target, the total integral dose (low dose regions) will become more. As a result using 6 MV means more beams which will lead to longer delivery times and increase the workload.

Gaining knowledge about the behaviour of the optimization parameters during optimization makes it easier to advise and assist the planner if a difficult IMRT plan is encountered; thus improving our turnaround time in our planning department. However this knowledge is not enough to decide which ICP is the best and can we confidently replace our "default" settings within our optimization process. While changing the parameters may result in more efficient optimisation, this must not come at the price of plan quality. The effect of these proposed changes on plan quality should therefore also be evaluated.

### 3.3.4 Beam quality indexing

From Section 3.2, it could be seen which ICP's are more suitable in terms of less MU's and fewer segments, however beam quality and delivery of the prescribed dose is an important aspect to consider. HI and CI were calculated for each plan which represents plan quality.

The calculation for HI and CI for Patient A is shown in Appendix B, Equation 2 and 3 were used.

Table 3.6 represents the results of the calculated HI and CI values for Patient A for 15 MV together with the total MU's and total number of segments, obtained from Table 3.2. Table 3.7 contains the results of 6MV for Patient A; the total MU's and total number of segments were obtained from Table 3.3. All four variables were normalized to the default plan.

*Table 3.6: Plan quality results normalized for all ICP, tabulated for Patient A, 15 MV, and including the default plan, as expressed in terms of total MU's and total number of segments, and showing quality measures HI and CI.*

| Patient A – 15 MV | | | | |
|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total no. of Segments** | **HI** | **CI** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.00 | 1.09 | 0.94 | 1.03 |
| 3 | 0.98 | 0.76 | 1.06 | 1.06 |
| 4 | 1.08 | 0.84 | 0.92 | 1.02 |
| 5 | 0.97 | 1.13 | 0.98 | 1.05 |
| 6 | 0.90 | 0.79 | 1.01 | 1.03 |
| 7 | 0.80 | 0.85 | 1.09 | 0.97 |
| 8 | 0.97 | 1.01 | 0.96 | 1.02 |
| 9 | 0.91 | 0.93 | 0.99 | 1.02 |
| 10 | 0.80 | 1.41 | 0.95 | 1.07 |
| 11 | 0.92 | 0.51 | 1.19 | 1.08 |
| 12 | 0.79 | 0.65 | 1.04 | 1.05 |
| 13 | 0.88 | 0.81 | 1.04 | 1.04 |
| 14 | 0.86 | 0.79 | 1.04 | 1.04 |
| 15 | 0.76 | 0.71 | 1.03 | 1.07 |
| 16 | 0.80 | 0.74 | 1.06 | 1.05 |

Note: HI is homogeneity index; CI is the conformity index.

*Table 3.7: Plan quality results normalized for all ICP, tabulated for Patient A, 6 MV, and including the default plan, as expressed in terms of total MU's and segments, and showing quality measures HI and CI.*

| Patient A – 6 MV | | | | |
|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total no. of Segments** | **HI** | **CI** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.14 | 1.10 | 0.96 | 1.05 |
| 3 | 1.14 | 0.79 | 1.09 | 1.08 |
| 4 | 1.20 | 0.84 | 0.91 | 1.06 |
| 5 | 1.09 | 1.24 | 1.04 | 1.06 |
| 6 | 1.06 | 0.90 | 1.03 | 1.04 |
| 7 | 0.92 | 0.88 | 1.06 | 1.00 |
| 8 | 1.10 | 1.01 | 0.98 | 1.04 |
| 9 | 1.08 | 0.94 | 1.11 | 0.98 |
| 10 | 0.82 | 0.91 | 0.99 | 1.09 |
| 11 | 1.00 | 0.50 | 1.19 | 1.09 |
| 12 | 0.84 | 0.75 | 1.09 | 1.08 |
| 13 | 0.91 | 0.87 | 1.09 | 1.06 |
| 14 | 0.91 | 0.85 | 1.08 | 1.06 |
| 15 | 0.88 | 0.81 | 1.04 | 1.09 |
| 16 | 0.85 | 0.75 | 0.97 | 1.08 |

Note: HI is homogeneity index; CI is the conformity index

Normalizing the results in Table 3.6 and Table 3.7 to the default plan (plan no. 1), made it easier to identify a more desirable plan, which will be a plan that has less MU's and total number of segments; has a smaller HI value and a larger CI value. According to Table 3.6 and Table 3.7, decreasing the IL from 7 to 5 resulted in a more homogenous plan and the MMUS optimisation parameter had the biggest influence on conformity of the PTV. Looking at Table 3.6 the plan nos. that mostly fulfil this more desirable plan criteria (as mentioned above) is plan nos. 3, 6, 7, 9 and 10 to 16. To determine if there is a correlation between MU's (Figure 3.6) and segments (Figure 3.7) versus the beam quality indices respectively, a Pearson Correlation Matrix was used to plot the data of the 15 clinical cases, only 15 MV data was used (15 MV is used clinically). A Pearson correlation value of 0 indicates that neither of the two variables plotted can be predicted from each other by a linear equation. A value of 1 or -1 indicates that there is perfect correlation and one variable can be predicted exactly from a linear equation.

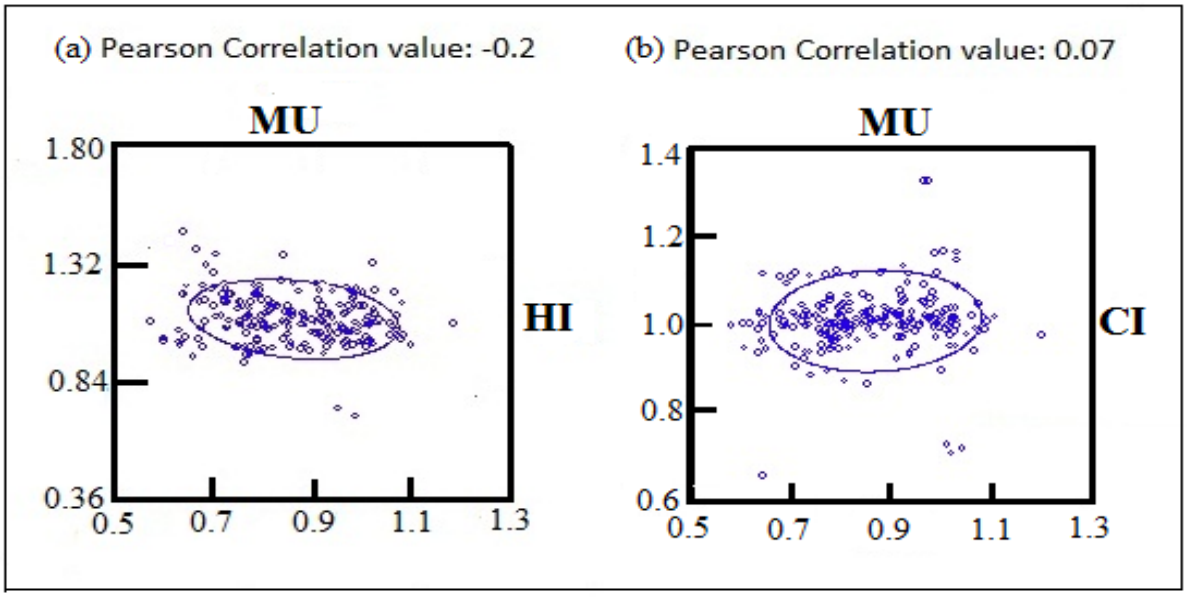



*Figure 3.6: (a) MU vs. HI as a beam quality variable for Patient A, 15 MV. (b) MU vs CI as a beam quality variable for Patient A, 15 MV.*

In Figure 3.6 it is seen that the MU variable, which can also be thought of as the delivered energy fluence, is not linearly related to the beam quality indexing variables, having a Pearson correlation value of -0.2 for MU's vs. HI and a value of 0.07 for MU vs. CI. This means that the delivered energy fluence are independent does not influence the quality of the plan.

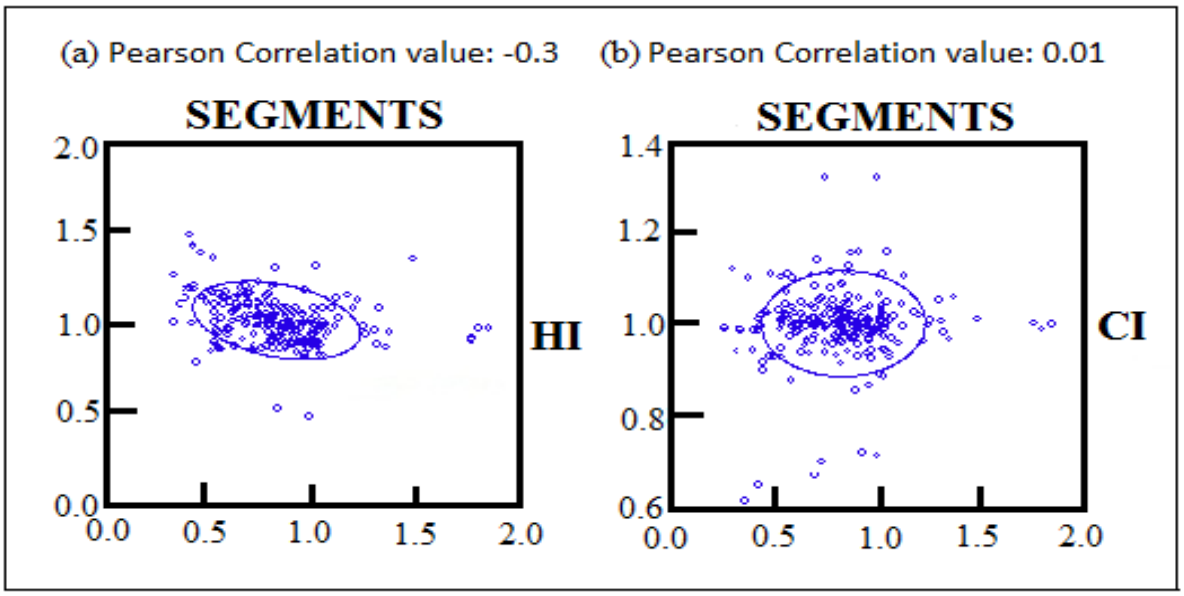



*Figure 3.7: (a) Segments vs. HI as a beam quality index for Patient A, 15 MV. (b) Segments vs. CI as a beam quality index for Patient A, 15 MV.*

Again in Figure 3.7, no linear correlation is seen between the segments and the beam quality variables. For segments vs. HI the Pearson correlation value was -0.3 and for the segments

vs. CI the value was 0.01. Having thus shown that the MU's and segments do not have a strong relationship with HI and CI, it is important to include them further on in the study as they contribute independent information in terms of plan quality.

This far the study has shown using the optimization parameters are an option to achieve a more conformal treatment plan. However two important aspects that are not demonstrated by these beam quality parameters; are delivery time and efficiency of a treatment plan. These aspects will be addressed in the next few chapters.

## 3.4 Summary

Re-optimizing IMRT prostate plans by varying some of the optimization parameters one at a time revealed important information in terms of the plan quality of each parameter. This made it possible to influence the outcome of an IMRT treatment plan by decreasing the total MU's and total number of segments. Having a treatment plan with fewer MU's and segments than our default plan, implies the possibility of creating a less complex IMRT plan with improved delivery efficiency. However fewer MU's and segments alone does not give an indication of plan quality, which is the most important aspect of a treatment plan, thus HI and CI are introduced as plan quality indicators. Knowing that MU and segments are not linearly related to HI and CI, all four variables will be used further on in this study to recommend a more efficient ICP. It is also clear that delivery time will be an important factor in deciding upon an efficient ICP for our institution, because we are not using IGRT (implanting fiducial markers) to track intra-fractional movement. As mentioned in chapter 1, intra-fractional movement becomes significant around 7 to 9.5 minutes[19] and can be calculated with a delivery time model[21]. Thus delivery time will be considered as the fifth variable to determine the top 10 ICP's and calculated in the next chapter.

# Chapter 4

## 4 Time delivery model

### 4.1 Introduction

From the literature[19] it is seen that intra-fractional movement becomes significant around 7 to 9.5 minutes. Thus, the delivery time component will possibly be the fifth variable in the analysis of the plans to determine which optimisation parameters will reliably produce an ideal ICP. To calculate the time delivery for the ICP's, a time delivery model is needed and as far as could be determined from the literature, a time delivery model has not yet been derived for a Siemens® ARTISTE™ 160-leaf linac. A time delivery model for step and shoot IMRT was created by Li and Xing for a Varian linac[21]and altered by Mittauer et al[22] for an Elekta linac. Using the principle of this model, a time delivery model was derived in this study for a Siemens® ARTISTE™ 160-leaf linac. Our model will be more global due to considering the RF warm-up time and including the MLC delay component.

### 4.2 Method

#### 4.2.1 Deriving the time delivery model

The time delivery model for the Varian linac was changed by adding the radio frequency (RF) wave warm-up factor and calculating the MLC travel time differently, by adding the MLC delay factor. For Siemens accelerators the RF wave time warm-up of 3 s is significant[49]compared to that of the Varian linac's of 0.5 s.

The model created for the Siemens® ARTISTE™ therefore consists of five parts (1) beam-on time, (2) gantry rotation time, (3) extra time for gantry rotation due to acceleration and deceleration before starting and stopping at the required angles, relative to a constant gantry speed, (4) extra time due to the radio frequency (RF) wave warm-up time before each beam starts, and (5) MLC travel time. Time delivery (T) can be obtained from the time delivery model defined in Equation as:

$$T \approx \frac{MU}{DR} + \left[T_G \text{ x } \left(1 - \frac{1}{N_B}\right)\right] + [\Delta T_G \text{ x } (N_B - 1)] + [RF \text{ x } (N_B)] + T_{MLC} \quad (4)$$

where: MU is total monitor units per fraction

DR is the dose rate

$T_G$ is the time required for the gantry to rotate 360°

$N_B$ is the total number of beams

$\Delta T_G$ is the extra time required for gantry acceleration and deceleration before starting and stopping

RF is the warm-up time required until beam-on is achieved for the beams ($N_B$)

$T_{MLC}$ is the MLC travel time and can be obtained as in Equation 5.

The MLC travel time ($T_{MLC}$) consists of two parts (Equation 5); firstly the field size in the direction of the moving leaves of the treatment plan is taken into account and secondly the effect of the total number of segments is taken into account. The total number of segments is subtracted from the total beams because MLC's move to the first segment position while the gantry moves. The first beam is subtracted from the total beams because the leaves defining the segments are already in place when radiation is switched on for first beam.

$$T_{MLC} = \frac{(FS \times N_B)}{MLC_{speed}} + \left[MLC_{delay} \text{ x } (N_s - (N_B - 1))\right] \quad (5)$$

where: FS is the average field size in the leaf direction of the treatment plan

$MLC_{speed}$ is the leaf travel speed

$MLC_{delay}$ is inter-segmental beam-on delay

$N_s$ is the total number of segments

$N_B$ is the total number of beams

### 4.2.2 Machine specific parameters

Table 4.1 gives an overview of all specific related parameter values that are needed for the time delivery model. Some of the values for machine parameters, such as the $MLC_{speed}$, $MLC_{delay}$, $T_G$, $\Delta T_G$ and RF wave, were physically confirmed by measurement on the Siemens® ARTISTE™ linac with a high performance *WIN* stopwatch and an estimate of the error on the readings was made. Although accuracy of the stopwatch is given as 1/100 second the response time was taken as 1/10 seconds.

*Table 4.1: Listing of Machine specific parameters determined in this study.*

| Name | Symbol |
|---|---|
| Dose Rate | DR |
| Gantry speed | $T_G$ |
| Gantry delay | $\Delta T_G$ |
| MLC Speed | $MLC_{speed}$ |
| MLC delay | $MLC_{dealy}$ |
| Radio frequency wave warm-up | RF |

Note: Machine specific parameters are corresponding to the Siemens® ARTISTE$^{TM}$ 160 MLC Leaf Linac.

The machine parameters determined were measured three times and the average was used. The machine parameters were measured as follows:

i. $MLC_{speed}$; a MLC box shaped field was set up on the linac with a 5 cm length in the leaf direction. The time it took for the leaves to travel 5 cm was measured 3 times and the average was divided by 5 to obtain travel speed which is expressed as cm/s.
ii. $MLC_{delay}$; time which it takes for all leaves to move into the next segment position and be verified against the treatment plan.
iii. $T_G$; Gantry was turned 200° counter clockwise starting at 30° and ending at 190°, however the stopwatch was only started to measure at gantry position 20° and ended at 200° position, thus gantry deceleration and acceleration were not included. The measured times were then multiplied by 2 to give the time to rotate 360°.
iv. $\Delta T_G$; is the deceleration time and was measured at various angles. Measurement started when gantry speed changed (slowed) and stopped after the gantry reached the desired angle. The value was multiplied by 2 to account for the acceleration as well. The deceleration and acceleration speed is the same; these settings were verified with the linac technician.
v. RF wave: time was measured from when "RAD ON" button was pressed on the linac console computer until dose delivery started.

All other machine specific parameters in Table 4.1 were obtained from the Siemens accelerator catalogue[50].

### 4.2.3 Verifying the time delivery model

The time delivery model was verified with ten arbitrarily (convenience sampling) selected prostate IMRT treatment plans. The delivery time of these plans were measured on the linac, with the *WIN* stopwatch. The measurements were repeated three times on different days. Before all measurements the gantry was turned to the starting angle; 306°. The measured time started after the "RAD ON" button was pressed at the linac console to start the beam delivery and stopped after the last segment's MU was delivered. The average measured time was compared to the calculated time.

To indicate if there is correlation between the measured and calculated data, the data was plotted and a linear regression line was obtained. The chi-squared test was also performed. If a correlation is found, the delivery times of all the ICP's generated in Chapter 3, Section 3.3.2 will be calculated. The time delivery component will then be included as the fifth variable.

## 4.3 Results and Discussion

### 4.3.1 Machine specific parameters

The machine-specific parameters are compared with the Siemens specifications, in Table 4.2. All measured values in Table 4.2 were used for the calculations, and the uncertainties within the measured parameters used in the model are used to calculate an absolute error estimate for the calculated time delivery.

*Table 4.2: Listing of the Machine specific input values for the derived time delivery model as compared to the specified values.*

| **Machine specific** | | |
|---|---|---|
| **Symbol** | **Measured Value** | **Siemens specification**[49,50] |
| **DR** | 533 ± 2.0 MU/min for 15 MV | 500 MU/min for 15 MV |
| **DR** | 333 ± 2.0 MU/min for 6 MV | 300 MU/min for 6 MV |
| $\mathbf{T_G}$ | 81.8 ± 0.2 s | |
| $\mathbf{\Delta T_G}$ | 6.6 ± 0.6 s | |
| **RF** | 3 ± 0.4 s | 3 – 6 s |
| $\mathbf{MLC_{speed}}$ | 1.3 ± 0.1 cm/s | Maximum 4 cm/s |
| $\mathbf{MLC_{delay}}$ | 2.5 ± 0.1 s | |

Note: DR, dose rate, $T_G$, gantry rotation for 360°, RF, radio frequency, $MLC_{speed}$, leaf speed, $MLC_{delay}$, intersegmental beam-on delay, $\Delta T_G$, gantry acceleration and deceleration before starting and stopping.

### 4.3.2 Calculating the time delivery model

Equation 4 and 5 were used for calculating the time delivery for ten randomly selected prostate IMRT treatment plans. These ten patients (Patient 1 to 10) are not the same as those that have been used in chapter 3. All input values, such as the MU, $N_S$, $N_B$ and FS were obtained from the treatment plan and Table 4.2. The calculation of the time delivery and absolute error of Patient 1 is shown in Appendix C. All calculated values were rounded to the nearest 1/10 second. Table 4.3 contains the results of all ten calculated prostate IMRT treatment plans.

### 4.3.3 Measuring the time delivery model

The same ten selected prostate IMRT treatment plans, for which the calculated delivery times in Section 4.3.2 were calculated, were used. Their delivery times were measured on the linac, in QA mode, meaning that no dose contribution was made to the treatment plans. The plans were measured on different days and the average is used for comparison. The standard deviation of the three measurements were taken as the error, see Table 4.3 for the tabulated measured and calculated values of these ten prostate IMRT plans.

*Table 4.3: The measured and calculated delivery time results for the ten prostate 15 MV IMRT treatment plans, with the uncertainty given as the standard deviations of the readings.*

| Patient No. | Total no. of MUs' | Total no. of Segments | Average Field Size ($cm^2$) | Average Measured time (s) | Calculated time (s) | Difference given as a % |
|---|---|---|---|---|---|---|
| 1 | 637 | 82 | 16 | 463 ± 1.5 | 479 ± 11 | 3.3 ± 2.6 |
| 2 | 618 | 72 | 15.45 | 437 ± 2.1 | 449 ± 9 | 2.7 ± 2.7 |
| 3 | 514 | 65 | 13 | 393 ± 2.1 | 406 ± 9 | 3.2 ± 2.8 |
| 4 | 561 | 62 | 13.6 | 391 ± 1 | 388 ± 8 | 0.8 ± 2.5 |
| 5 | 765 | 58 | 14.24 | 384 ± 1.5 | 383 ± 8 | 0.3 ± 2.5 |
| 6 | 453 | 51 | 10.33 | 322 ± 3.2 | 333 ± 7 | 3.3 ± 3.1 |
| 7 | 667 | 78 | 16.6 | 469 ± 2 | 475 ± 11 | 1.3 ± 2.7 |
| 8 | 580 | 62 | 15.8 | 389 ± 1.5 | 400 ± 9 | 2.8 ± 2.7 |
| 9 | 431 | 52 | 10.8 | 314 ± 2.1 | 317 ± 7 | 0.9 ± 2.8 |
| 10 | 755 | 87 | 15.2 | 480 ± 1.5 | 479 ± 11 | 0.2 ± 2.6 |
| | | | | **Overall average % difference:** | | **1.9** |

The uncertainty for the measured values is the average of the 3 measurements. The uncertainty for the calculated values is the calculated relative error within the measured Machine input parameters.

The response time with the stopwatch was 1/10 second which was also taken as the absolute error for the measured data. The delivery time measured ranged between 314 s and 480 s, (5 to 8 minutes) for the ten patients. The largest percentage difference between the measured and calculated times was 3.3% (16 s) and the smallest 0.3% (1 s). The average percentage difference was 1.9%. Li and Xing[21] estimated an average of 2.1% difference with their time delivery model (created for a Varian linac), with their largest difference at 3.9% (16 s). The time delivery model created for an Elekta linac, Mittauer et al. (2013)[22], gave their biggest difference at 5.7% (10 s). Thus our results obtained from our proposed derived time delivery model agrees well with other delivery models found in the literature. Adding the RF and $MLC_{delay}$ component makes our model more widely applicable to most accelerators.

The IMRT prostate plan with the largest percentage difference was the plan with the least segments and smallest field size. For this case the time delivery model overestimated the time, thus the calculated time was more than the measured time. Overestimation of the time delivery model was also seen for the IMRT prostate plan with the most segments. The $MLC_{delay}$ and $MLC_{speed}$ component of the time delivery model contains the biggest uncertainty, which represent the segment delivery part.

### 4.3.4 Verifying the time delivery model

A correlation plot (Figure 4.1) was done between the measured and calculated delivery times to verify the time delivery model, Equation 4 (Section 4.2.1). The values tabulated in Table 4.4 were used to do the correlation with.

*Table 4.4: Input values for the correlation plot to verify the time delivery model*

| Plan No. | Measured (s) | Calculated (s) |
|---|---|---|
| **1** | 463 | 479 |
| **2** | 437 | 449 |
| **3** | 393 | 406 |
| **4** | 391 | 388 |
| **5** | 384 | 383 |
| **6** | 322 | 333 |
| **7** | 469 | 475 |
| **8** | 389 | 400 |
| **9** | 314 | 317 |
| **10** | 480 | 479 |

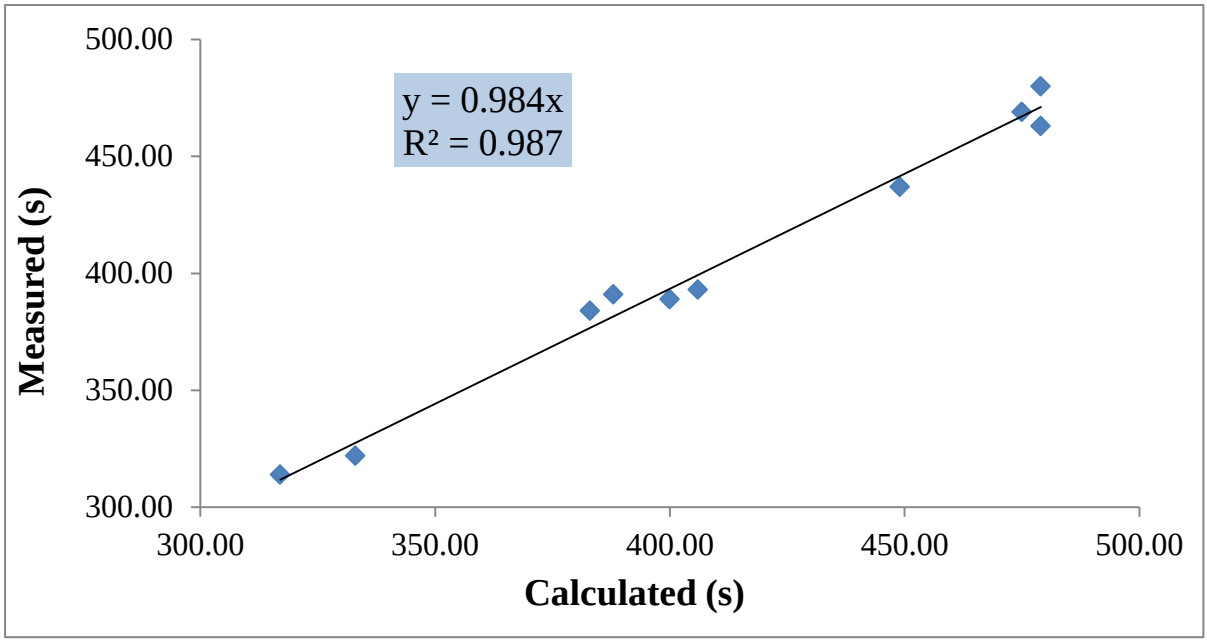



*Figure 4.1: Correlation between Measured and Calculated delivery times*

The linear regression value of 0.987 indicates that there is a strong linear correlation between the measured and calculated delivery times (Table 4.3).

The chi-squared test ($\chi^2$) is performed as well to determine how far away the measured ($y$) and calculated ($x$) delivery times are in terms of a standard deviation[51]. For each $x$ value it is possible to calculate and predict a $y$ value by using a predicted model $y = f(x)$ as seen in Figure 4.1, and then compare the actual $y$ value using the $\chi^2$ test. Our calculated $\chi^2$ probability value is 0.99, calculated with Excel, thus the model does fit our data and it is possible to predict the measured delivery times from the calculated delivery times.

## 4.4 Delivery time as a variable

In Section 4.3.4 the derived time delivery model was verified and concluded that the model can be used with confidence. The delivery time was calculated for all ICP's and included as a variable to determine the top 10 ICPs. Table 4.5 indicates the calculated delivery time for Patient A (15 MV) as a variable together with the plan quality variables tabulated in Table 3.6. All five variables were calculated and normalized for all 15 patients and tabulated in Appendix D.

*Table 4.5: All five variables calculated for Patient A, 15 MV ICP's.*

| Patient A | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total no. of Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.00 | 1.09 | 0.94 | 1.03 | 1.03 |
| 3 | 0.98 | 0.76 | 1.06 | 1.06 | 0.90 |
| 4 | 1.08 | 0.84 | 0.92 | 1.02 | 0.95 |
| 5 | 0.97 | 1.13 | 0.98 | 1.05 | 1.05 |
| 6 | 0.90 | 0.79 | 1.01 | 1.03 | 0.90 |
| 7 | 0.80 | 0.85 | 1.09 | 0.97 | 0.91 |
| 8 | 0.97 | 1.01 | 0.96 | 1.02 | 1.00 |
| 9 | 0.91 | 0.93 | 0.99 | 1.02 | 0.96 |
| 10 | 0.80 | 1.41 | 0.95 | 1.07 | 1.13 |
| 11 | 0.92 | 0.51 | 1.19 | 1.08 | 0.80 |
| 12 | 0.79 | 0.65 | 1.04 | 1.05 | 0.83 |
| 13 | 0.88 | 0.81 | 1.04 | 1.04 | 0.91 |
| 14 | 0.86 | 0.79 | 1.04 | 1.04 | 0.90 |
| 15 | 0.76 | 0.71 | 1.03 | 1.07 | 0.85 |
| 16 | 0.80 | 0.74 | 1.06 | 1.05 | 0.86 |

Note: HI is the homogeneity index, CI is the conformity index. The values were normalized to the default plan.

From Table 4.5, it is seen that the longest and shortest time component correlated with the most and least total number of segments, plan no. 10 and no. 11 respectively. The relationship between these two variables (segments and time delivery) is indicated in Figure 4.2.

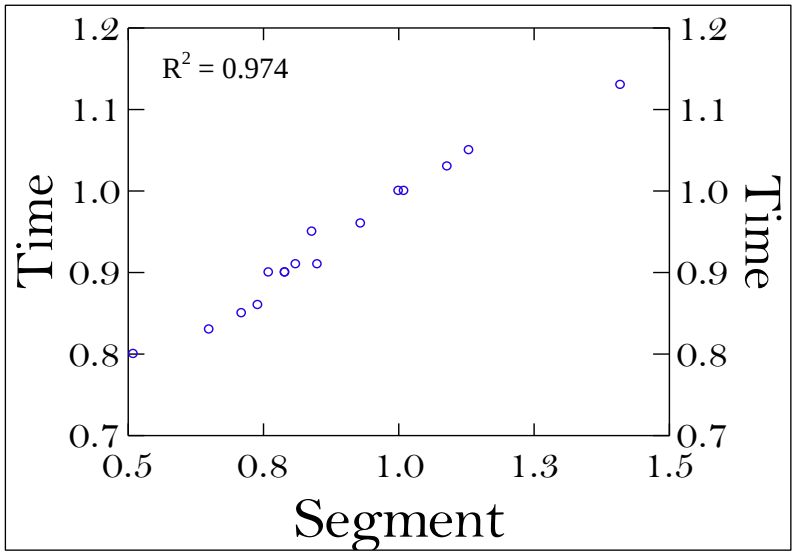



*Figure 4.2: Plot showing that the relationship between the number of segments and the time delivery variables is linear.*

There is a linear relation ($R^2$ = 0.974) between the total number of segments and delivery time variables, Figure 4.2. This means that the inter-segmental (segment movement) time has a bigger influence on a treatment plan than the intra-segmental (dose delivery) time. To obtain a faster deliverable plan, it is recommended that the total number of segments of an IMRT plan should be minimized.

## 4.5 Summary

A time delivery model was successfully derived and verified for a Siemens® ARTISTE™ linac. The derived model incorporates the RF delay time as well as MLC delay component, making this model more applicable to most linac's. Knowing the delivery time beforehand makes it possible to distinguish between the efficiencies of treatment plans and even different techniques. It will be possible to give an oncologist more information regarding delivery efficiency; making the best clinical decision regarding treatment delivery for a patient. In a clinical environment this is important because intra-fractional movement increases with longer delivery times. Advanced techniques such as VMAT and IMRT are composed of integrated steps; MLC movement, gantry movement and dose rate fluctuations. Knowing the delivery time of a treatment plan beforehand makes it possible to explore the time component as a quality control parameter during treatment in future.

Up to this point within the study four variables represented the plan quality component of the ICP's. Although the time delivery and segment variables are linearly related, the time delivery component will now also be included as the fifth variable for this study, as knowledge (within 2%) delivery time of an ICP is valuable. The delivery time can influence a clinical decision in terms of which plan is chosen to be treated. We need to remember that the variables are therefore not independent.

# Chapter 5

## 5 K-means Clustering

### 5.1 Introduction

In the previous chapters five variables namely; MU, segments, HI, CI and delivery time were identified and calculated for each ICP (Table 4.5) generated in Section 3.3.2. In this Chapter, 10 of the 15 ICP's which generally fulfil the set criteria below will be identified; these top 10 ICP's will be used further on in the study. The criteria for choosing these 10 ICP's are (compared to the default plan):

1. The total MU's should be decreased
2. There should be fewer total number of segments
3. The HI value should be lower
4. The CI value should be higher
5. And it should be delivered faster than the average plan.

On initial assessment all the 15 re-optimized ICP's to the default plan seemed viable. But what was desired was a stable group of ICP's within the data, those that fulfil the criteria the best. As it was not certain where the default plan (plan no. 1) lay in comparison to the other plans as assessed using the above criteria; a cluster analysis model program was used to determine if there was any clustering of the data and how the plans were distributed in relationship to each other.

Cluster analysis is a multivariate procedure for detecting a natural grouping in data[52,53,54]. A set of data will be divided into non-over lapping groups. In this study the k-means clustering algorithm will be used. This algorithm partition *N* objects into *k* groups simultaneously. These groups are centred around k points which are the means of each group, hence the name k-means clustering. The data within each group or cluster should share the same characteristics. For this algorithm the characteristics are quantified in terms of Euclidean distance (shortest distance between two points). This means that values of each *n* objects within the same cluster will all have a 'close numeric value' in a set of dimensions and the within-group sum of squares is minimized. The formula for Euclidean distance (d) between a point X ($X_1$, $X_{2\ldots}$) and a point Y ($Y_1$, $Y_2\ldots$) is:

$$d = \sqrt{\sum_{i=1}^{n}(x_i - y_i)^2} \quad \ldots (6)$$

The ICP plans generated for each patient were divided into different groups when the cluster analysis method is used. The 5 variables mentioned above are the dimensions of each plan and are used to calculate the variations between and within the clusters. A statistical program MYSTAT version 12 was used to do the cluster analysis.

## 5.2 Method

### 5.2.1 K-means clustering

When using k-means clustering, the total number of subgroups, or clusters, can be selected before commencement of the procedure. A histogram of the data was drawn to detect the number of natural peaks and it was decided to utilise 5 groups (clusters).

The data were normalized to the default plan, because standardizing the data is important when doing cluster analysis, it puts the data on a common scale. The k-means clustering option was chosen in MYSTAT program and the 5 variables were set as objectives with 20 iterations and 5 cluster groups selected as indicated by Figure 5.1 and Figure 5.2.

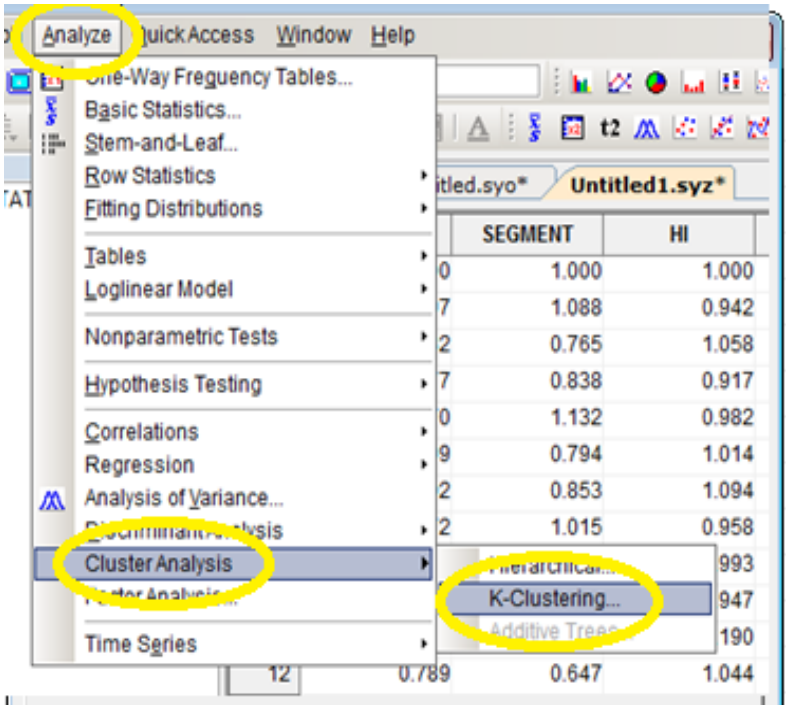



*Figure 5.1: Interface Display of the Cluster Analysis option in MYSTAT program, selecting the K-Clustering option to do analysis of the data.*

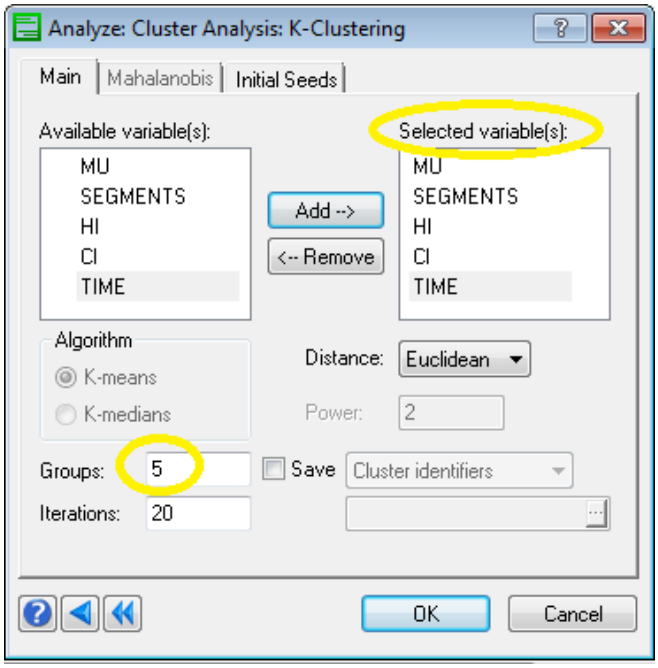



*Figure 5.2: Interface display showing that the five variables for a 5 group selection were set within the K-Clustering tab option in MYSTAT program.*

The outcome was given as a cluster SPLOM (Scatterplot Matrix) and a cluster profile set, indicated by Figure 5.3 and Figure 5.4. The cluster profile indicates where each variable's data point lies in terms of the average of that cluster. It was possible to identify which plan numbers belong to which cluster profile group. MYSTAT program is Excel based and the tabulated results of all the patients could be imported into the program from Excel.

The total plans (450 plans) generated in Section 3.3.1 were divided into different Data Set groups to allow effective interpretation of the data during cluster analysis. The different Data Set groups are as follows:

I. All data points with normalized plans – all 465 plans (including default plans)
II. All data points without the normalized plans – 450 plans (excluding default plans)
III. Data points of 6 MV plans only – 240 plans (including the 15 default plans)
IV. Data points of 15 MV plans only – 240 plans (including the 15 default plans)
V. Data points of plans with PTV > 900 cc – 160 plans
VI. Data points of plans with PTV < 150 cc – 224 plans
VII. Data points of plans with 70 Gy prescription – 64 plans
VIII. Data points of plans with 60 Gy prescription – 224 plans
IX. Data points of plans with 50 Gy prescription – 192 plans
X. Data points of plans with 7 fields (both energies) – 224 plans
XI. Data points of plans with 6 fields (both energies) – 256 plans

The results of the cluster profile plot and a scatterplot matrix (SPLOM) for the cluster groups (1 to 5) were obtained for each Data Set Group. The cluster groups 1 to 5 which contained the preferred plan criteria (explained in Section 5.1) were noted. The plan numbers which occurred in the preferred cluster groups of 1 to 5 were exported into Excel. The frequency distribution tool within Excel was used to indicate the frequency of a plan number occurring in the desired cluster profile group. Only the 15 MV plans were considered in determining the top 10 ICP's because only 15 MV beams are currently used for treatment in our Institution.

## 5.3 Results and Discussion

### 5.3.1 K-means clustering

K-means clustering was performed on the different data set groups mentioned in Section 5.2.1. The SPLOM of Data Set I (all the data point) is indicated by Figure 5.3. The behaviour of each cluster group could be seen for example, the cluster group 3 (green points) which appeared to contain the outliers. However it was not possible to decide which cluster groups are the best from the SPLOM, for this the cluster profile plot was needed; Figure 5.4.

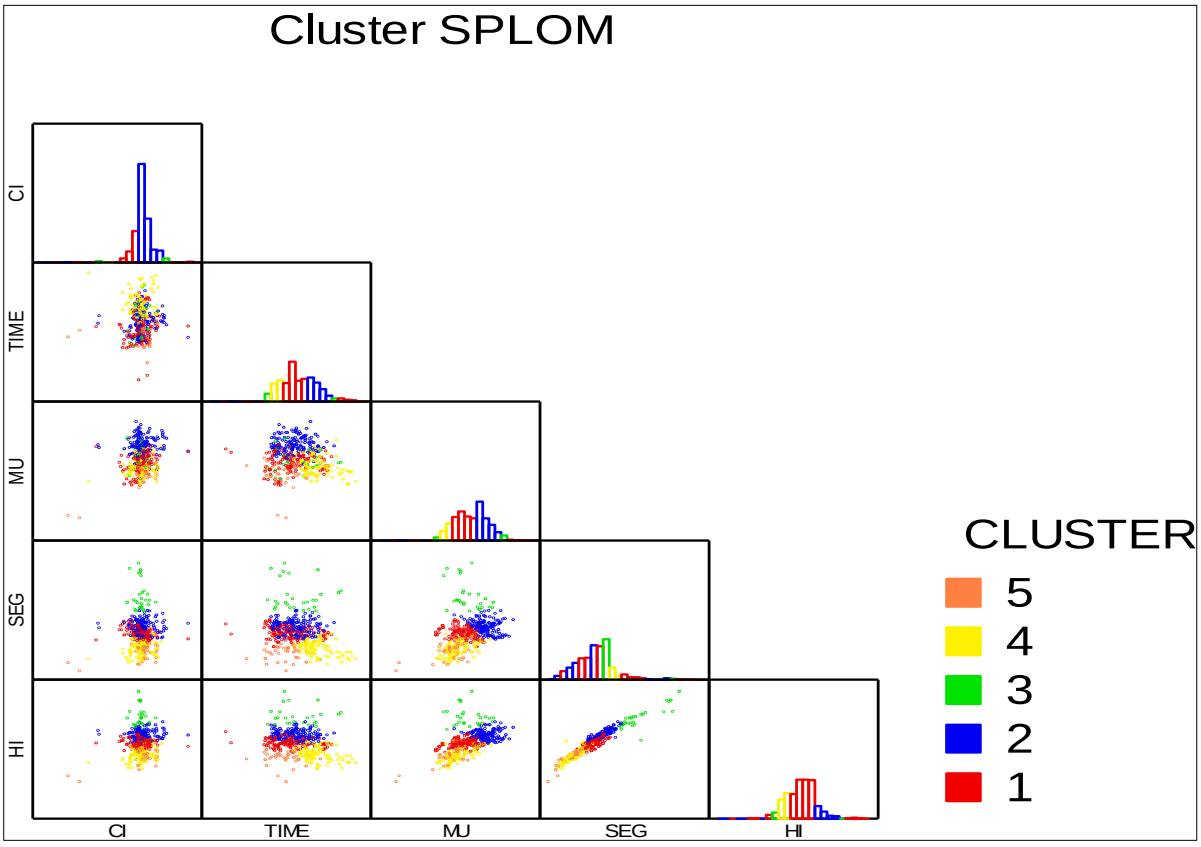



*Figure 5.3: The cluster scatterplot matrix (SPLOM) groups the data of the five variables which are most alike for Data Set group I together, using five cluster groups. Cluster group no. 3 (green) seems to contain the outlier data which are far from the major clustered grouping.*

The cluster profile plot of the Data Set groups I to IV is displayed in Figure 5.4. The dotted black line indicates the average value of that Data Set group. The blue line indicates the value range of each variable within that cluster group. We are looking for a cluster group where the MU, segments, HI and the time delivery variable have smaller values than the average (dotted black line), while the CI variable should have a value bigger than the average. For Data Set I, cluster group 4 and 5 were chosen as the groups that contain the variables that mostly fulfil the criteria. Using the frequency distribution tool within Excel it could be seen how frequently a plan number occurs in a certain group as indicated by Table 5.1. This approach was used for all the Data Set groups this principle was used.

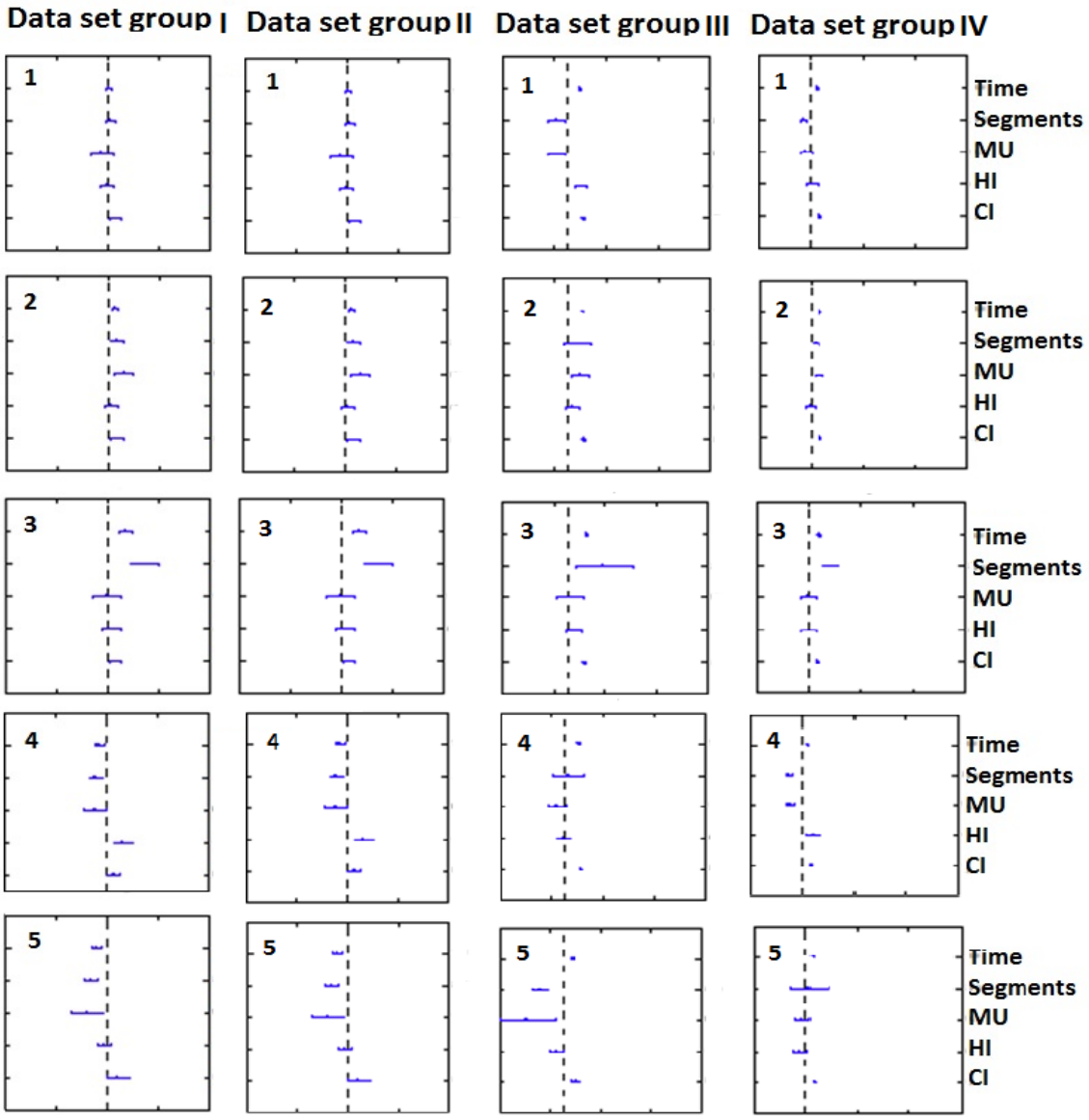



*Figure 5.4: Cluster profile plots of the five cluster groups in the Data Set groups I to IV. The dotted black line indicates the average value of that cluster group. The blue line represents the value range of each variable.*

Considering the cluster profile plots for Data Set I and II, no differences are seen in the cluster groups. Meaning that the normalized plans (defaults plan) can be included while clustering is done, the normalized plans do not obscure the outcome. From this point onward all the default plans of each patient were included during the analysis.

Considering the cluster groups 1 to 5 for Data Set I and II (Figure 5.4), the ideal plans; having less MU's and segments, deliver treatments faster and having dose distributions which conform better to the tumour, will lie in cluster group 4 and 5.

Investigating the cluster groups 1 to 5 for Data Set III (6 MV plans) and IV (15 MV plans), the ideal plans will lie in cluster groups 1, 4 and 5. This is interesting because Data set I is a combination of Data set III and IV for which the ideal plans occurred in cluster groups 4 and 5. This can be due to the difference in total number of plans within the Data Set groups; if the initial partitions are different than the result in final clusters are different. This is a disadvantage of the k-means clustering algorithm. Clustering was done on all the Data Set groups I – XI (Appendix E contains all cluster profiles).

*Table 5.1: The frequency of plan numbers occurring in each Data Set group, according to the selected cluster groups within the cluster profile plots.*

| **Plan** | **DATA SET GROUP** | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **No.** | I | II | III | IV | V | VI | VII | VIII | IX | X | XI |
| **1** | 0 | 0 | 0 | 0 | 0 | 10 | 0 | 0 | 0 | 1 | 0 |
| **2** | 0 | 0 | 1 | 3 | 2 | 0 | 0 | 0 | 0 | 0 | 3 |
| **3** | 9 | 9 | 7 | 9 | 3 | 0 | 3 | 1 | 1 | 2 | 6 |
| **4** | 1 | 1 | 3 | 5 | 2 | 4 | 0 | 0 | 0 | 1 | 5 |
| **5** | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 2 |
| **6** | 3 | 3 | 5 | 8 | 5 | 0 | 2 | 1 | 1 | 4 | 6 |
| **7** | 0 | 0 | 8 | 10 | 4 | 3 | 3 | 2 | 2 | 4 | 7 |
| **8** | 0 | 0 | 2 | 4 | 4 | 2 | 0 | 0 | 0 | 0 | 4 |
| **9** | 0 | 0 | 6 | 5 | 3 | 0 | 2 | 0 | 0 | 0 | 6 |
| **10** | 4 | 4 | 3 | 5 | 0 | 0 | 3 | 3 | 3 | 12 | 2 |
| **11** | 30 | 27 | 15 | 15 | 10 | 3 | 4 | 7 | 7 | 14 | 16 |
| **12** | 23 | 23 | 14 | 15 | 9 | 14 | 4 | 6 | 6 | 13 | 15 |
| **13** | 18 | 17 | 12 | 15 | 9 | 14 | 4 | 5 | 5 | 12 | 14 |
| **14** | 20 | 19 | 14 | 14 | 10 | 10 | 4 | 4 | 4 | 12 | 15 |
| **15** | 18 | 17 | 13 | 15 | 10 | 10 | 4 | 4 | 4 | 13 | 16 |
| **16** | 18 | 18 | 15 | 15 | 10 | 11 | 4 | 4 | 4 | 12 | 16 |

Note: I – All data points with normalized plans (included default plans), II - All data points without the normalized plans (excluded default plans), III - Data points of 6 MV plans only, IV - Data points of 15 MV plans only, V - Data points of plans with PTV > 900 cc, VI - Data points of plans with PTV < 150 cc, VII - Data points of plans with 70 Gy prescription, VIII - Data points of plans with 60 Gy prescription, IX - Data points of plans with 50 Gy prescription, X - Data points of plans with 7 fields, XI - Data points of plans with 6 fields

Interpreting Table 5.1 should be done as follows: For Data Set group I, plan no. 3 occurred 9 times in the chosen cluster groups (4 and 5), while plan no. 11 occurred the most, thus fulfilling the set criteria the best.

For Data Set group III and IV almost the same plan numbers are favoured which means that the optimization parameters are not energy dependant and that the SMART segmentation method is better.

Comparing the results for Data Set V and IV (volume sizes), a difference in plan number frequency is seen, which means that the volume size of the target does have an influence on the optimization outcome. Plan no. 1 occurred in the Data Set group IV as favourable, which means that our current TPS optimization parameter values (default plan settings) favour small volumes. No big differences in the Data Set groups VII, VIII an IX (different prescription) are seen between the favoured plan numbers thus the total prescribed dose does not influence the optimization outcome. Looking at the cluster group 1 to 5 for these 3 Data Set groups the MU variable was an outlier, see Appendix E. Thus MU's are mostly influenced by the prescription. The last Data Set group comparison is X and XI (beam arrangement) which differed the most in terms of plan number favouring, which makes sense because the optimization algorithm will be influence by the beam arrangement; trying to avoid OARs and covering the target differently due to different incoming beams. Again the MU variable was seen as an outlier, thus beam arrangement will have an influence on total MU's as well.

Choosing the top 10 ICP's was done by looking at the 15 MV (Data Set Group IV), Table 5.2. Only 15 MV plans were considered, because currently 15 MV is been used clinically in our Institution. The plans were ranked according to frequency of occurrence as indicated by Table 5.2.

*Table 5.2: Plan numbers ranked for Data Set group IV (15 MV) according to the most favourable plan to fulfil the set criteria.*

| Plan No. | Frequency | Position Ranked |
|---|---|---|
| **11** | 15 | 1 |
| **12** | 15 | 2 |
| **13** | 15 | 3 |
| **15** | 15 | 4 |
| **16** | 15 | 5 |
| **14** | 14 | 6 |
| **7** | 10 | 7 |
| **3** | 9 | 8 |
| **6** | 8 | 9 |
| **9** | 5 | 10 |
| **4** | 5 | 11 |
| **10** | 5 | 12 |
| **8** | 4 | 13 |
| **2** | 3 | 14 |
| **1** | 0 | 15 |
| **5** | 0 | 16 |

Plan numbers 11 to 16 were ranked at the top position. Plan numbers 9, 4 and 10 had the same frequency occurrence of 5, however only 10 ICP's are chosen for measurement. It was decided to use plan number 9, because within the 6 MV Data Set group, plan number 9 occurred more frequently than plan number 4 and 10. Thus plan numbers, 11, 12, 13, 14, 15, 16, 14, 7, 3, 6, 9 was selected as the top ten ICP's.

## 5.4 Summary

The k-means clustering analysis method is a suitable way to group data points which have similar characteristics. A few observations can be made regarding our data. MU was seen as an outlier for different prescriptions. This means that for the same beam arrangement and beam energy, total MU's will vary for different prescribed target doses. Moret et al. concluded that the risk of producing secondary induced cancers is proportional to the beam on time or total MU's .[23] For us in our department this means; if we would like to increase target dose prescription we will need to use a different beam arrangement. Changing beam arrangement angles can cover the target more optimally and not necessarily increase MU's. Although more beams will decrease the total MU's, it is not recommended as this will increase delivery time. This is confirmed by the cluster analysis results for which the total MU's was again seen as an outlier by the observation of beam arrangement Data Set group X and XI. Up to this point we worked towards an ideal ICP, thus recommending a set of ideal optimization parameter values to improve planning efficiency and plan quality. However from the results it has been observed that our current default optimization parameter settings (plan no. 1) favour smaller volume sizes of the target (< 150 ml). Thus maybe it will not be possible to recommend only one set of optimization parameters for prostate IMRT.

We also need to consider that thus far the optimization parameter outcomes were only analysed in terms of their behaviour towards a suitable clinical outcome and it did not take delivery efficiency into account. Delivery efficiency is an important aspect of the study because having a well conformed treatment plan does not imply that it will be delivered as expected or in an efficient manner on the linac. Thus what the oncologist sees on the TPS is not necessarily what the patient receives. The top 10 ICP's were identified through the cluster analysis method. These ICP's will be measured on a Siemens® ARTISTE™ linac (Chapter 6) to determine if they can be delivered accurately and efficiently.

# Chapter 6

## 6 Deliverability of the 10 IMRT combination plans

### 6.1 Introduction

Delivery efficiency indicates how accurately and quickly an IMRT plan can be delivered to the patient. Delivery efficiency will be determined by treatment time and any limitations that the linac may have such as inaccuracies of MLC movement and non-linear MU output. This is the last part of this study and will be done to investigate and confirm the final recommendations regarding the optimization parameters that need to be set to achieve the best ICP for prostate IMRT and also to determine if only one set of optimization parameters is sufficient.

### 6.2 Method

#### 6.2.1 MapCHECK2 measurements

The top 10 ICP's (Section 5.3.1) together with the default plan of three patients' (Patient L, M and N) with a 7 field beam arrangement (currently preferred clinical choice) were chosen to be measured three times through a step and shoot delivery technique. Measurements were repeated on different days to incorporate linac day-to-day variances. These patient's PTV sizes ranged between 48 and 130 ml. The reason for choosing patients with volume sizes below 150 ml will confirm if our default plan optimization settings is still favourable, as was observed during the k-means clustering analysis.

The dose fluences of these plans were measured with a 2D dose array device, called MapCHECK2, displayed in Figure 6.1. The MapCHECK2 consists of 1527 detector diodes positioned on a rectangular grid and uniformly spaced at 7.07 mm apart. The beams were measured in a planar manner. This is an accepted method for patient QA.[55] The measured data were then analysed by a 3D dose volume histogram (3DVH) program.

On the TPS a new QA plan was made for each of the selected 10 ICP's, the default plan was also included for measurement, to compare delivery efficiency with current clinic treatment choice. The beams were recalculated in a 30 x 30 $cm^2$ Perspex phantom, all beam gantry angles were turned to 0° for planar measurements. Transverse dose fluences for each beam were exported at 5 cm depth. These new QA plans were then imported into our Record and Verify system. Each beam could be downloaded individually and delivered on the linac.

The software called Sun Nuclear Corporation (SNC) Patient version 6.2.3 of Sun Nuclear was opened and connected to the MapCHECK2 device. On the linac the MapCHECK2 was setup at 98.65 cm source to surface distance (SSD). A spirit level is used to level the detector. The inherent Perspex build-up of the MapCHECK2 is 1.7 cm. A total of 4.4 cm Perspex is used (add 2.7 cm Perspex) to calibrate the diodes to 5 cm water equivalent dose. A dose of 100 MU was delivered and the absolute dose file was saved. The new measured dose file together with the relevant array calibration file was chosen. Before patient dose fluences could be measured, the Perspex build-up was changed to 3.3 cm to equal the same depth of 5 cm Perspex at which the TPS dose fluences were exported. Each beam was delivered on the linac and saved.

After all 11 plans (top 10 ICPs and default plan) per patient were delivered and saved in the SNC patient software, comparison was done per beam between the measured and TPS dose fluence. A 3 mm and 3% distance to agreement (DTA) was used, which is what we are currently using in practice. Although ICRU 83 recommends a criterion of 3 mm and 5% for low gradient regions, it was felt that this is not strict enough to distinguish between the delivered plans. The DTA criteria means that when comparing a point, $a_m$ (measured fluence) and point $a_{TPS}$ (TPS fluence); the dose difference will be $D(a_m) - D(a_{TPS})$, if it is $\leq 3\%$ that point will pass. Looking at 3 mm criteria means that $D(a_m+r) = D(a_{TPS})$, thus if the radius (r) is less than 3 mm, the measuring dose distribution will pass at that point.

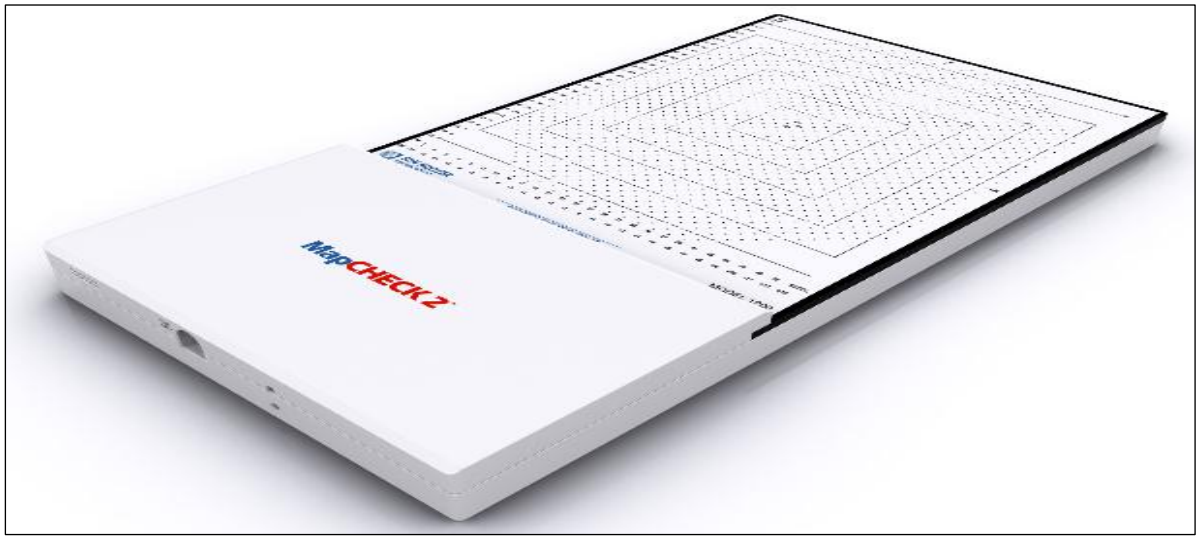



*Figure 6.1: MapCHECK2 device consisting of detector diodes was used for 2D planar measurements.*

### 6.2.2 3D Volume histogram analysis

The 3DVH program of Sun Nuclear version 2.11 was used to analyse the results in a 3D manner, meaning that the results obtained from the 2D array are projected onto the CT of the patient with delineated structures. In SNC Patient software (MapCHECK2's software) a planned dose perturbation (PDP) file was written which compared the measured fluences with the TPS's fluences per beam. The PDP file was exported and saved. Together with the CT images, structure set, treatment plan and dose file, the PDP file was imported into the 3DVH program. Again a passing criterion of 3% and 3 mm DTA was used. Reporting the results includes the % pass rate values (% of voxels in the structure that pass with the criteria) obtained for the PTV 1, PTV 2, rectum, bladder and femoral heads.

## 6.3 Results and Discussion

Firstly the linac MLC variation was investigated by comparing Patient L's day-to-day measurements, indicated by Table 6.1. These results represent the planar measurement, thus the percentage difference of the measured fluences compared to the TPS's fluence at 5 cm depth. The other two patients' results of the measurement can be found in Appendix G.

The three measurements for Patient L (Table 6.1) indicated that there is a drift in the MLC's between measurements. Comparing the percentage pass rate value of the three measurements of field 1 of the default plan; 88.2%, 92.8% and 92.8% respectively, indicates that the first set of measurements differed by 5%. This big difference was not only due to MLC variation, but also due to a MLC leaf-bank motor which was replaced after the first set of measurements. Comparing the second and third set percentage pass rate values for the rest of the plans revealed differences of no more than 3%. Mechanical variations of the linac do have an influence on the percentage pass rate values. However our set criteria are 3% and 3 mm, taking most of these linac limitations into account.

*Table 6.1: Measurement results using a 3% and 3mm agreement between measured fluences obtained with the MAPCHECK2 and TPS fluences of all three measurements.*

| **Measurement 1** | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Plan No.** | Field 1 (%) | Field 2 (%) | Field 3 (%) | Field 4 (%) | Field 5(%) | Field 6 (%) | Field 7 (%) |
| **Default** | 88.2 | 93.1 | 87.4 | 85.8 | 92.0 | 85.4 | 92.3 |
| **3** | 90.8 | 91.7 | 90.3 | 86.5 | 91.7 | 86.2 | 89.0 |
| **6** | 91.8 | 92.6 | 93.5 | 90.4 | 91.9 | 90.2 | 91.3 |
| **7** | 96.9 | 97.4 | 95.1 | 95.0 | 97.0 | 94.4 | 92.9 |
| **9** | 91.1 | 94.4 | 94.0 | 92.6 | 95.7 | 89.8 | 95.3 |
| **11** | 95.6 | 93.1 | 97.8 | 84.6 | 90.5 | 95.3 | 95.9 |
| **12** | 92.8 | 92.7 | 87.6 | 90.1 | 95.8 | 92.0 | 94.3 |
| **13** | 93.1 | 91.5 | 90.3 | 87.2 | 96.4 | 92.8 | 95.2 |
| **14** | 94.7 | 91.0 | 90.7 | 90.7 | 94.9 | 92.0 | 95.2 |
| **15** | 93.9 | 96.3 | 87.9 | 92.2 | 94.4 | 91.4 | 92.6 |
| **16** | 91.5 | 90.7 | 90.7 | 89.7 | 88.7 | 91.3 | 89.7 |
| **Measurement 2** | | | | | | | |
| **Plan No.** | Field 1 | Field 2 | Field 3 | Field 4 | Field 5 | Field 6 | Field 7 |
| **Default** | 92.8 | 93.2 | 92.4 | 88.3 | 94.0 | 88.8 | 89.6 |
| **3** | 95.2 | 93.2 | 92.4 | 87.4 | 90.2 | 86.2 | 85.9 |
| **6** | 95.0 | 93.8 | 93.1 | 89.3 | 94.1 | 89.8 | 87.9 |
| **7** | 97.8 | 94.1 | 91.9 | 95.3 | 94.4 | 91.2 | 92.3 |
| **9** | 92.0 | 94.7 | 96.2 | 93.3 | 94.4 | 91.0 | 94.1 |
| **11** | 96.2 | 95.1 | 99.1 | 86.1 | 93.1 | 97.0 | 95.9 |
| **12** | 95.6 | 93.2 | 94.3 | 90.1 | 94.2 | 91.6 | 92.8 |
| **13** | 95.9 | 88.7 | 96.2 | 90.7 | 97.6 | 93.1 | 96.3 |
| **14** | 96.6 | 89.9 | 95.0 | 93.3 | 95.2 | 91.9 | 94 |
| **15** | 95.7 | 94.9 | 90.7 | 92.4 | 91.9 | 94.3 | 93.4 |
| **16** | 96.0 | 94.3 | 93.5 | 90.9 | 91.6 | 94.6 | 93.2 |
| **Measurement 3** | | | | | | | |
| **Plan No.** | Field 1 | Field 2 | Field 3 | Field 4 | Field 5 | Field 6 | Field 7 |
| **Default** | 92.8 | 92.9 | 94.6 | 88.3 | 95.2 | 88.2 | 91.9 |
| **3** | 95.7 | 93.8 | 94.0 | 88.0 | 92.7 | 88.4 | 90.5 |
| **6** | 96.0 | 96.4 | 95.5 | 91.6 | 95.1 | 89.9 | 90.5 |
| **7** | 98.8 | 97.2 | 95.3 | 97.1 | 97.0 | 91.8 | 94.6 |
| **9** | 94.0 | 96.7 | 94.5 | 94.1 | 95.6 | 91.3 | 95.5 |
| **11** | 96.5 | 93.9 | 98.4 | 87.7 | 92.8 | 97.6 | 96.5 |
| **12** | 95.9 | 93.8 | 93.0 | 90.1 | 94.2 | 92.5 | 95.1 |
| **13** | 95.6 | 92.1 | 94.0 | 89.5 | 97.3 | 92.8 | 96.8 |
| **14** | 95.9 | 89.8 | 95.3 | 93.3 | 95.2 | 92.8 | 94.0 |
| **15** | 95.4 | 96.9 | 86.4 | 93.9 | 96.7 | 91.3 | 89.7 |
| **16** | 96.0 | 91.0 | 88.4 | 91.8 | 88.4 | 90.4 | 88.8 |

Table 6.2 to Table 6.7 respectively indicate the average percentage pass rate of the three measurements for Patient L, Patient M and Patient N of each plan. The top 3 highest percentage pass rate averages for each patient are underlined.

*Table 6.2: Tabulated the average and standard deviation of the percentage pass rate of the three measurements for Patient L.*

| **Patient L** | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Plan No. | Field 1 | Field 2 | Field 3 | Field 4 | Field 5 | Field6 | Field7 | Avg. % Pass Rate per plan |
| Default | 91.3±2.7 | 93.1±0.2 | 91.5±3.7 | 87.5±1.4 | 93.7±1.6 | 87.5±1.8 | 91.3±1.5 | 90.8±2.2 |
| 3 | 93.9±2.7 | 92.9±1.1 | 92.2±1.9 | 87.3±0.8 | 91.5±1.3 | 86.9±1.3 | 88.5±2.3 | 90.5±2.6 |
| 6 | 94.3±2.2 | 94.3±1.9 | 94.0±1.3 | 90.4±1.2 | 93.7±1.6 | 90.0±0.2 | 89.9±1.8 | 92.4±2.0 |
| 7 | 97.8±1.0 | 96.2±1.9 | 94.1±1.9 | 95.8±1.1 | 96.1±1.5 | 92.5±1.7 | 93.3±1.2 | 95.1±2.8 |
| 9 | 92.4±1.5 | 95.3±1.3 | 94.9±1.2 | 93.3±0.8 | 95.2±0.7 | 90.7±0.8 | 95.0±0.8 | 93.8±1.6 |
| 11 | 96.1±0.5 | 94.0±1 | 98.4±0.7 | 86.1±1.6 | 92.1±1.4 | 96.6±1.2 | 96.1±0.3 | 94.2±3.8 |
| 12 | 94.8±1.7 | 93.2±0.6 | 91.6±3.6 | 90.1±0.1 | 94.7±0.9 | 92.0±0.5 | 94.1±1.2 | 92.9±1.6 |
| 13 | 94.9±1.5 | 90.8±1.8 | 93.5±3 | 89.1±1.8 | 97.1±0.6 | 92.9±0.2 | 96.1±0.8 | 93.5±2.6 |
| 14 | 95.7±1.0 | 90.2±0.7 | 93.7±2.6 | 92.4±1.5 | 95.1±0.2 | 92.2±0.5 | 94.4±0.7 | 93.4±1.8 |
| 15 | 95.0±1.0 | 96.0±1 | 88.3±2.2 | 92.8±0.9 | 94.3±2.4 | 92.3±1.7 | 91.9±1.9 | 93.0±2.3 |
| 16 | 94.5±2.6 | 92.0±2 | 90.9±2.6 | 90.8±1.1 | 89.6±1.8 | 92.1±2.2 | 90.6±2.3 | 91.5±1.5 |

*Table 6.3: Tabulated average and standard deviation for the percentage pass rate of the three measurements for Patient M.*

| Patient M | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Plan No. | Field 1 | Field 2 | Field 3 | Field 4 | Field 5 | Field6 | Field7 | Avg. % Pass Rate per plan |
| Default | 93.6±0.6 | 93.2±1.8 | 92.7±2.4 | 91.1±1.3 | 93.3±0.9 | 87.9±3.3 | 92.4±0.4 | 92.0±2.0 |
| 3 | 93.2±1.3 | 89.6±3.0 | 90.1±2.6 | 89.4±1.2 | 92.2±2.5 | 85.6±2.9 | 92.4±1.7 | 90.4±2.6 |
| 6 | 93.9±0.8 | 91.1±2.0 | 92.5±3.7 | 90.7±0.6 | 94.0±2.1 | 89.8±2.0 | 94.2±0.7 | 92.3±1.8 |
| 7 | 95.0±1.7 | 94.8±0.9 | 94.3±1.8 | 94.0±0.8 | 95.7±0.6 | 93.8±1.4 | 93.7±0.8 | 94.5±0.7 |
| 9 | 87.8±1.3 | 94.2±1.6 | 94.8±1.0 | 93.4±0.9 | 95.6±2.0 | 93.9±0.9 | 96.2±1.0 | 93.7±2.8 |
| 11 | 93.8±0.5 | 93.4±0.9 | 97.3±1.1 | 91.3±1.5 | 90.0±0.3 | 90.7±1.8 | 95.8±2.4 | 93.2±2.7 |
| 12 | 92.3±0.5 | 96.1±0.3 | 93.8±0.8 | 86.1±1.0 | 96.2±2.5 | 94.0±2.8 | 95.0±1.2 | 93.4±3.5 |
| 13 | 92.4±0.3 | 94.9±1.0 | 90.3±2.4 | 86.4±1.8 | 96.4±0.8 | 94.3±2.3 | 96.1±0.7 | 93.0±3.6 |
| 14 | 44.0±2.1 | 38.0±4.0 | 41.5±3.1 | 41.7±2.2 | 43.1±2.4 | 43.6±2.5 | 38.5±3.1 | 41.5±2.4 |
| 15 | 93.8±0.1 | 92.8±1.1 | 94.6±0.5 | 90.9±0.6 | 88.1±1.9 | 91.0±2.1 | 95.7±0.9 | 92.4±2.6 |
| 16 | 91.5±1.4 | 91.9±1.6 | 96.4±1.5 | 93.0±3.3 | 94.9±1.6 | 93.4±1.9 | 95.1±1.0 | 93.7±1.8 |

*Table 6.4: Tabulated average and standard deviation of the percentage pass rate of the three measurements for Patient N.*

| Patient N | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Plan No. | Field 1 | Field 2 | Field 3 | Field 4 | Field 5 | Field6 | Field7 | Avg. % Pass Rate per plan |
| Default | 92.4±1.4 | 94.2±1.2 | 94.3±2.8 | 90.8±1.0 | 91.7±1.1 | 87.4±1.9 | 94.1±1.1 | 92.1±2.5 |
| 3 | 92.9±2.2 | 92.3±1.9 | 92.9±3.4 | 92.6±3.5 | 87.7±4.2 | 82.9±2.4 | 88.9±1.4 | 90.0±3.8 |
| 6 | 93.5±0.9 | 92.5±1.5 | 93.8±3.5 | 91.6±2.6 | 92.3±2.2 | 86.2±1.8 | 90.1±3.6 | 91.4±2.6 |
| 7 | 92.3±4.8 | 95.0±3.8 | 95.4±3.4 | 93.7±4.0 | 93.1±4.1 | 89.0±3.9 | 93.0±1.8 | 93.1±2.1 |
| 9 | 95.1±3.8 | 95.4±2.3 | 93.2±3.2 | 94.7±2.2 | 94.0±1.2 | 90.2±2.1 | 94.5±1.3 | 93.9±1.8 |
| 11 | 93.3±1.9 | 94.4±3.0 | 98.0±2.1 | 79.9±3.2 | 98.7±0.6 | 95.6±2.0 | 94.9±3.2 | 93.5±6.3 |
| 12 | 92.3±1.8 | 97.1±0.2 | 93.3±1.2 | 95.7±1.2 | 94.0±0.2 | 92.0±1.9 | 95.7±2.8 | 94.3±1.9 |
| 13 | 93.2±0.5 | 96.4±0.8 | 98.3±0.4 | 92.4±2.0 | 94.8±0.4 | 91.0±1.4 | 95.3±1.8 | 94.5±2.5 |
| 14 | 94.6±3.7 | 96.6±0.7 | 98.3±0.4 | 92.3±1.4 | 94.9±0.5 | 91.3±1.2 | 94.9±2.1 | 94.7±2.4 |
| 15 | 90.7±2.5 | 95.6±1.0 | 97.1±0.6 | 95.7±1.5 | 93.4±0.8 | 95.0±1.3 | 97.5±1.4 | 95.0±2.3 |
| 16 | 93.1±2.0 | 94.1±3.4 | 96.3±0.7 | 94.0±0.6 | 96.1±0.2 | 89.9±3.0 | 93.7±1.0 | 93.9±2.1 |

As indicated by Table 6.2 to Table 6.4, the top 3 plans which had the highest percentage pass rate for Patients L, M and N respectively were plan nos. 7, 9 and 11; plan nos. 7, 9 and 16 and plan nos. 13, 14 and 15. Although plan nos. 7 and 9 appeared twice with the highest pass rate between the three patients, it is important to remember that these comparisons are only at 1 depth. The results can easily be misinterpreted due to false positive or false negative interpretation; meaning that a lower pass rate can be falsely positive because the lower percentage pass rate area can be over an OAR area, which will be preferred[55].

Clearly the importance of analysing the results in a 3D manner is apparent[56,57], and for this the 3DVH program of Sun Nuclear will be used.

### 6.3.1 3D Volume histogram analysis

A PDP file was calculated from the measured data for each patient. This PDP file together with the CT images, dose file, treatment plan and structure set was loaded into the program and a comparison was done. The difference between the measured and exported TPS fluences is displayed on the CT image of the patient (Figure 6.2). In the histogram blue areas indicate voxels that measured lower than the criteria and red areas indicate areas that measured above the set criteria as indicated by Figure 6.2.

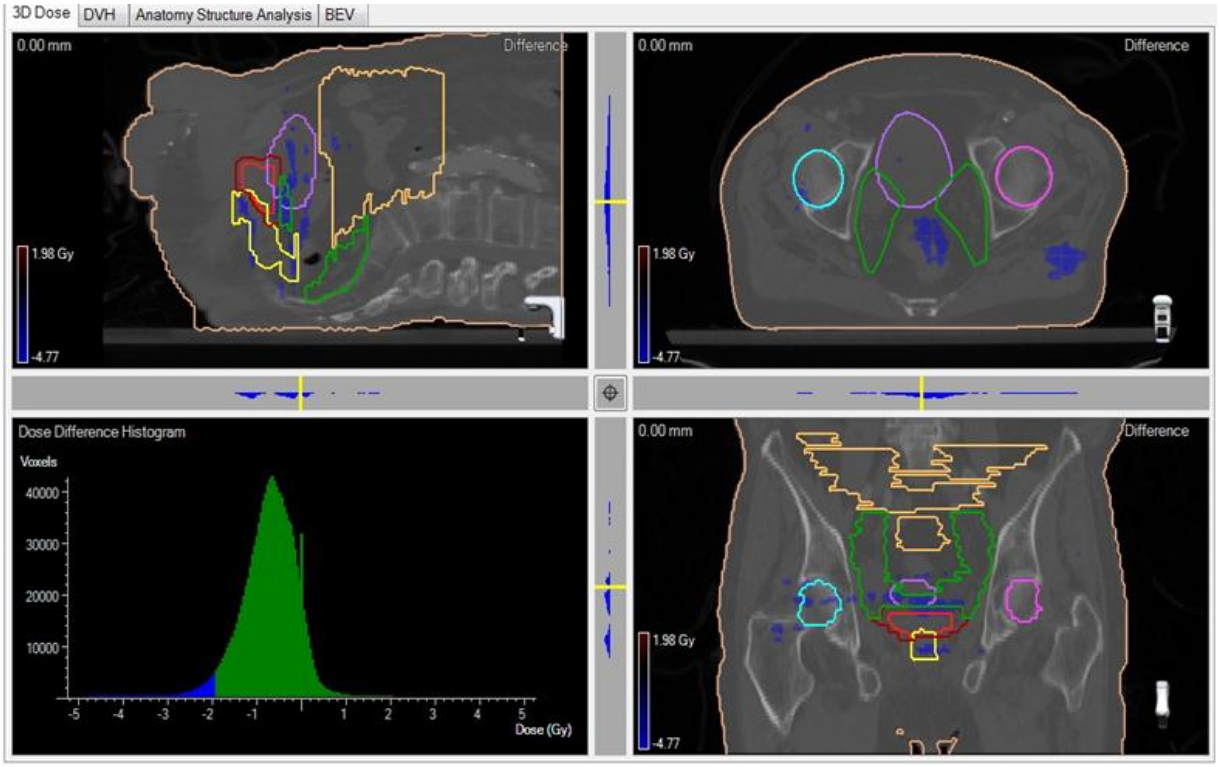



*Figure 6.2: In the 3DVH program the dose difference (blue areas lower and red areas higher) between measured and TPS's fluences are displayed on the CT images of the patient (Patient L), making it possible to analyse the Patient QA in a 3D manner.*

The 3DVH program also creates a report representing the percentage pass rate for each structure which was drawn in on the TPS; it displays the total voxels/points that measured lower or higher than the set criteria (3% and 3 mm). With this information it is possible to evaluate each ICP in a different manner, meaning that we can compare the PTV coverage and not only fluence at one depth. Using this report the percentage pass rate of the PTV 1, PTV 2, bladder, rectum and Left and Right femoral heads was noted. This information is important to decide which ICP has the best delivery efficiency. The results of the structures mentioned above for all ICP's measured for the 3 patients are compiled in Table 6.5 to Table 6.7.

*Table 6.5: Percentage pass rate of delineated structures of Patient L for all ICP's measured; including the percentage of the voxels measured higher and lower than the set criteria.*

| **Patient L** | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | **Plan no.** | | | | | | | | |
| **Structures** | **Default** | **3** | **6** | **7** | **9** | **11** | **12** | **13** | **14** | **15** | **16** |
| **PTV1** | 76.1 | 99 | 99 | 99.9 | 99.4 | 94.5 | 99.8 | 95.4 | 99.4 | 100 | 99.9 |
| Higher | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0.1 |
| Lower | 23.9 | 1 | 1 | 0.1 | 0.6 | 5.5 | 0.2 | 4.6 | 0.6 | 0 | 0 |
| **PTV2** | 90.4 | 90.8 | 90.2 | 92.8 | 91.8 | 89.7 | 91.4 | 90.3 | 91.1 | 93 | 84.6 |
| Higher | 0 | 3 | 3.3 | 0.2 | 0.5 | 0 | 0 | 0 | 0 | 0 | 9.4 |
| Lower | 9.6 | 6.2 | 6.5 | 7 | 7.7 | 10.3 | 8.6 | 9.7 | 8.9 | 7 | 6 |
| **Rectum** | 87 | 94.4 | 94.7 | 94.6 | 93.5 | 89.4 | 85.6 | 86 | 87.6 | 93.5 | 92.8 |
| Higher | 0 | 0 | 0.8 | 2.6 | 0 | 0 | 0 | 0 | 0 | 0 | 2 |
| Lower | 13 | 5.6 | 4.5 | 2.8 | 6.5 | 10.6 | 14.4 | 14 | 12.4 | 6.5 | 5.2 |
| **Bladder** | 64.1 | 86.1 | 90.6 | 98.1 | 89.8 | 77.5 | 79.1 | 73.6 | 77.1 | 89.7 | 97.8 |
| Higher | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Lower | 35.9 | 13.9 | 9.4 | 1.9 | 10.2 | 22.5 | 20.9 | 26.4 | 22.9 | 10.3 | 2.2 |
| **L Femoral Head** | 85.6 | 98.8 | 99.5 | 100 | 98.5 | 100 | 100 | 99.3 | 99.7 | 100 | 100 |
| Higher | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Lower | 14.4 | 1.2 | 0.5 | 0 | 1.5 | 0 | 0 | 0.7 | 0.3 | 0 | 0 |
| **R Femoral Head** | 92.4 | 99.8 | 100 | 100 | 99.6 | 99.7 | 100 | 99.8 | 100 | 100 | 100 |
| Higher | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Lower | 7.6 | 0.2 | 0 | 0 | 0.4 | 0.3 | 0 | 0.2 | 0 | 0 | 0 |

Table 6.5 represents the data of Patient L for different structures. The most important structure is PTV 1 and PTV 2 and should be covered by 100%, meaning that all voxels within that structure should fulfil the 3% and 3 mm criteria. The OAR such as the rectum, bladder and femoral heads should measure as low as possible and be within QUANTEC recommendations. It is not advisable to compromise the target, which is PTV 1 and PTV 2 to

insure the OAR receive a lower dose. In Table 6.5 to Table 6.7, the focus was on the best coverage of PTV 1 and PTV 2. All of the OARs did fulfil QUANTEC recommendations. Looking at the percentage pass rate of the PTV 1 in Table 6.5, Plan nos. 3, 6, 7, 9, 15 and 16 did cover PTV 1 at least 99%. Focusing on PTV 2 for Patient L, Plan nos. 3, 6, 15 and 16 covered the PTV 2 the best with at least 94%, plan nos. 7 and 9 covered the PTV 2 with 93%. It was interesting to see that plan nos. 3, 6, 15 and 16 had voxels that measured higher than the set criteria within the PTV 2; having hot spots in the target; this represents a poor HI. Concluding that plan nos. 7 and 9 will be the preferred option for treatment.

*Table 6.6: Percentage pass rate of delineated structures of Patient M for all ICP's measured; including the percentage of the voxels measured higher and lower than the set criteria.*

| **Patient M** | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | **Plan No.** | | | | | | | | | |
| **Structures** | **Default** | **3** | **6** | **7** | **9** | **11** | **12** | **13** | **14** | **15** | **16** |
| **PTV1** | 98 | 99.9 | 100 | 99.8 | 100 | 99.8 | 99 | 99.7 | 3 | 99.7 | 100 |
| Higher | 0 | 0.1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Lower | 2 | 0 | 0 | 0.2 | 0 | 0.2 | 1 | 0.3 | 97 | 0.3 | 0 |
| **PTV2** | 93.3 | 77.4 | 91 | 94.7 | 91.8 | 93.3 | 91.7 | 92.4 | 1 | 90.8 | 90.1 |
| Higher | 0 | 18.6 | 4.2 | 1.3 | 3.7 | 0.9 | 0 | 0.3 | 0 | 4.3 | 6.3 |
| Lower | 6.7 | 4 | 4.8 | 4 | 4.5 | 5.8 | 8.3 | 7.3 | 99 | 4.9 | 3.6 |
| **Rectum** | 94.7 | 98.4 | 95.7 | 99.7 | 98 | 95.3 | 90.7 | 93.6 | 6.6 | 92.8 | 99.7 |
| Higher | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Lower | 5.3 | 1.6 | 4.3 | 0.3 | 2 | 4.7 | 9.3 | 6.4 | 93.4 | 7.2 | 0.3 |
| **Bladder** | 88.1 | 99.3 | 97.9 | 99.6 | 98.9 | 90.4 | 87.2 | 92.3 | 0.6 | 97.7 | 99.9 |
| Higher | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Lower | 11.9 | 0.7 | 2.1 | 0.4 | 1.1 | 9.6 | 12.8 | 7.7 | 99.4 | 2.3 | 0.1 |
| **L Femoral Head** | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 23 | 100 | 100 |
| Higher | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Lower | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 77 | 0 | 0 |
| **R Femoral Head** | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 18 | 100 | 100 |
| Higher | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Lower | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 82 | 0 | 0 |

Looking at the results of Table 6.6 for Patient M, almost all of the ICP's covered the PTV 1 with at least 99.7%, except the default plan and plan no. 14. Plan no. 14 measured very low all 3 times. Investigating the coverage of PTV 2 revealed again that most of the plans had hot spots in the target, however plan nos. 7 and 11 had the least hot spots; 1.3% and 0.9%

respectively, but plan no. 7 has a higher coverage of almost 96%, thus plan no. 7 will be treatment of choice.

*Table 6.7: Percentage pass rate of delineated structures of Patient N for all ICP's measured; including the percentage of the voxels measured higher and lower than the set criteria.*

| **Patient N** | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | **Plan No.** | | | | | | | | | |
| **Structures** | **Default** | **3** | **6** | **7** | **9** | **11** | **12** | **13** | **14** | **15** | **16** |
| **PTV1** | 96.7 | 99.9 | 100 | 99.5 | 95.1 | 82 | 77 | 89.6 | 88.9 | 88.8 | 70.9 |
| Higher | 0 | 0.1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Lower | 3.3 | 0 | 0 | 0.5 | 4.9 | 18 | 23 | 10.4 | 11.1 | 11.2 | 29.1 |
| **PTV2** | 92.6 | 91.7 | 92 | 94.3 | 93.5 | 77.1 | 83 | 84 | 83.9 | 88.1 | 85 |
| Higher | 0 | 3.3 | 3.2 | 0.1 | 0 | 11.3 | 0 | 0 | 0 | 0 | 0 |
| Lower | 7.4 | 5 | 4.8 | 5.6 | 6.5 | 11.6 | 17 | 16 | 16.1 | 11.9 | 15 |
| **Rectum** | 95.6 | 99.9 | 99 | 100 | 98.2 | 94.4 | 79.3 | 83.4 | 83.3 | 85 | 82.5 |
| Higher | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Lower | 4.4 | 0.1 | 1 | 0 | 1.8 | 5.6 | 20.7 | 16.6 | 16.7 | 15 | 17.5 |
| **Bladder** | 94.7 | 99.3 | 99.1 | 99 | 98.5 | 81.9 | 70 | 62.3 | 61.8 | 90.7 | 79.3 |
| Higher | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Lower | 5.3 | 0.7 | 0.9 | 1 | 1.5 | 18.1 | 30 | 37.7 | 38.2 | 9.3 | 20.7 |
| **L Femoral Head** | 99.7 | 100 | 100 | 100 | 100 | 98 | 100 | 100 | 100 | 100 | 100 |
| Higher | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| Lower | 0.3 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| **R Femoral Head** | 99.1 | 100 | 99.8 | 100 | 100 | 99.8 | 100 | 100 | 100 | 100 | 100 |
| Higher | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Lower | 0.7 | 0 | 0.2 | 0 | 0 | 0.2 | 0 | 0 | 0 | 0 | 0 |

Looking at the results of Table 6.7 for Patient N, it seems that only plan nos. 3, 6 and 7 managed to cover PTV 1 with at least 99%. Plan nos. 3 and 6 again had hot spots (not a good HI) in the PTV 2 of at least 3%. Plan no. 7 will again be the treatment of choice; covering the PTV 2 with at least 94%. As mentioned before although some of the OAR does measure higher within certain plans the entire OAR group for these 3 patients was within tolerance.

Concluding from these 3 patients it seems that plan no. 7 (General High filter) will be the treatment of choice. Although these 3 patients have the same prescription and beam arrangement the volume size did differ and ranged between 48 to 130 cc. As previously mentioned, volume size of the target does influence the optimization outcome in terms of favouring the default plan no. 1, but after taking into account the linac limitations is seems that plan no. 7 is most deliverable. The optimization parameter of plan no. 7 was to add a

General High filter to the optimization process. The smoothing filter parameter is the only optimization parameter that is introduced during the initial optimization (Figure 1.1), while all other optimization parameters are introduced during the segmentation process.

To obtain an efficient deliverable IMRT prostate treatment plan it is important to create a less complex IMRT plan. This can be done by introducing the General High filter parameter during the optimization process. Such an IMRT plan may not conform tide around the target on the TPS due to fewer segments. However it is more important to know that the treatment plan seen on the TPS can be accurately delivered to the patient and all targets will be properly treated.

## 6.4 Summary

Measurements of the ICP's on the linac revealed information regarding the deliverability of dose fluences and MLC day-to-day variations. Measuring these QA dose fluences in a planar (2D) way can easily lead to misinterpretation of the results, due to false positive or false negative information. This means that a lower pass rate can be falsely positive if the lower percentage pass rate area is over an OAR area. This information was not sufficient to make a decision in terms of best delivery efficacy therefore the 3DVH program was used. It displays the dose fluences in a 3D manner, revealing information on every structure which was delineated. Using this information it was possible to establish that when the General High filter is added during the initial optimization process the best delivery efficiency is achieved. It was thus possible to recommend only one set of optimization parameter values for a prostate IMRT plan.

# Chapter 7

## 7 Conclusion

This study demonstrated that, by changing the optimization parameters during the planning process on a XiO TPS, a less complex IMRT plan can be created. Our goal was to recommend a set of planning parameters which would improve delivery efficiency while maintaining plan quality. It was shown that the MU and radiation therapy delivery efficiency for a prostate IMRT treatment plan can be improved by introducing a General High filter to the optimization process, thus meeting our goal. Our recommended settings for the optimization parameters during the optimization process for the SLW method using a fixed beam angle distribution of 51° between beams are: (i) MMUS set to 5, (ii) use 7 IL, (iii) MSS set as 2, and (iv) using the General High filter.

A limitation of this study is that the beam angle distribution was not investigated; because the focus of this study was to determine the optimization parameter behaviour during the inverse optimization process. The software being used did not include an option to optimise the angles used in the planning. From this study it was noted that beam geometry does influence the optimization outcome by decreasing the total MU's. In future studies, beam geometry should be investigated because total MU's are related to the risk of secondary induced cancers.

From the literature it is seen that there exist two strong opinions regarding which energy should be used, 6 or 15 MV, when treating prostate cancer. In our Institution 15 MV is used however in this study both energies were considered during the optimization process and it was concluded that the optimization parameters are not greatly influenced by the beam energy. Therefore it is possible to use the recommended optimization parameter settings if it should be decided to implement 6 MV as the treatment energy for prostate treatment in our Institution.

A time delivery model was derived and verified for a Siemens® ARTISTE$^{TM}$ linac. By including the RF warm-up wave component and the MLC delay factor in the proposed model, the derived time delivery model should be applicable to most linacs. In order to decrease delivery time, the total number of segments should be minimized. This can be done through changing some of the optimization parameters during the optimization process. Although the calculated results were found to be in line with those found in the literature, the

biggest uncertainty in the time delivery model calculated is found to be within the inter-segmental component. This uncertainty was less than 5%, which is in line with the uncertainties published in the literature and was therefore considered acceptable and was not investigated any further as 5 % would make a 15 s difference on a 5 minute treatment and this was felt to be acceptably small. Having a time delivery model available for a Siemens® ARTISTE$^{TM}$ linac makes it possible to explore the time delivery component in future as a potential quality control parameter.

Being able to deliver a prostate IMRT plan faster and still achieve acceptable delivery efficiency is valuable for departments with limited access to IGRT and which operate with linac's that have low dose rates.

Finally I would like to mention that the recommended optimization parameter values were implemented in our radiation therapy department and thus far no treatment plan done using the parameters recommended as a result of this study has been rejected by an oncologist and none has failed QA, which indicates that the proposed set of parameters is feasible for implementation in practice.

# Chapter 8

## 8 References


1. www.cancerresearchuk.org/cancer-info/cancerstats/wolrd/prostate-cancer-world/ Accessed September 2013.

2. www.prostatecancerfoundation.co.za/cake/app/webroot/index.php/pages.

3. Dolezel M, Odrazka K, Vaculikova M, et al. Dose escalation in prostate radiotherapy up to 82 Gy using simultaneous integrated boost: direct comparison of acute and late toxicity with 3D-CRT 74 Gy and IMRT 78 Gy. *Strahlenther Onkol*. 2010;186(4):197–202.

4. Forsythe K, Blacksburg S, Stone N, Stock RG. Intensity-modulated radiotherapy causes fewer side effects than three-dimensional conformal radiotherapy when used in combination with brachytherapy for the treatment of prostate cancer. *Int J Radiat Oncol Biol Phys*. 2012;83(2):630–5.

5. Uhl M, Van Triest B, Eble MJ, Weber DC, Herfarth K, De Weese TL. Low rectal toxicity after dose escalated IMRT treatment of prostate cancer using an absorbable hydrogel for increasing and maintaining space between the rectum and prostate: Results of a multi-institutional phase II trial. *Radiother Oncol*. 2013;106(2):215–219.

6. Takeda K, Takai Y, Narazaki K, et al. Treatment outcome of high-dose image-guided intensity-modulated radiotherapy using intra-prostate fiducial markers for localized prostate cancer at a single institute in Japan. *Radiother Oncol*. 2012:1–10.

7. Treutwein M, Hipp M, Kölbl O, Bogner L. IMRT of prostate cancer: a comparison of fluence optimization with sequential segmentation and direct step-and-shoot optimization. *Strahlenther Onkol*. 2009;185(6):379–83.

8. Lin C, Donaldson SS, Meza JL, et al. Effect of radiotherapy techniques (IMRT vs. 3D-CRT) on outcome in patients with intermediate-risk rhabdomyosarcoma enrolled in COG D9803--a report from the Children's Oncology Group. *Int J Radiat Oncol Biol Phys*. 2012;82(5):1764–70.

9. McCloskey S., Wollman RC, Rose CM, et al. Quality of Life (QOL) Outcomes After Three-Dimensional Conformal Radiation Therapy (3D-CRT) and Intensity Modulated Radiation Therapy (IMRT) for Localized Prostate Cancer. *Int J Radiat Oncol*. 2005;63:S113.

10. Pearlstein K, Chen RC. Comparing dosimetric, morbidity, quality of life, and cancer control outcomes after 3D conformal, intensity-modulated, and proton radiation therapy for prostate cancer. *Semin Radiat Oncol*. 2013;23(3):182–90.

11. Seco J, Sharp GC, Turcotte J, Gierga D, Bortfeld T, Paganetti H. Effects of organ motion on IMRT treatments with segments of few monitor units. *Med Phys*. 2007;34(3):923.

12. Huang E, Dong L, Chandra A, et al. Intrafraction prostate motion during IMRT for prostate cancer. *Int J Radiat Oncol Biol Phys*. 2002;53(2):261–8.

13. Bernchou U, Agergaard SN, Brink C. Radiopaque marker motion during pre-treatment CBCT as a predictor of intra-fractional prostate movement. *Acta Oncol (Madr)*. 2013;(November 2012):1168–1174.

14. Fortin I, Carrier F, Beauchemin C, Delouya G, Taussky D. Using fiducial markers in the prostate bed in postprostatectomy external beam radiation therapy improves accuracy over surgical clips. *Strahlentherapie und Onkol*. 2014;(May 2013):467–471.

15. Loh J, Baker K, Sridharan S, et al. Infections after fiducial marker implantation for prostate radiotherapy : are we underestimating the risks ? *Radiother Oncol*. 2015:1–6.

16. Deegan T, Owen R, Holt T, et al. Interobserver variability of radiation therapists aligning to fiducial markers for prostate radiation therapy. *J Med Imaging Radiat Oncol*. 2013;57:519–523.

17. Thompson A, Fox C, Foroudi F, et al. Planning and implementing an implanted fiducial programme for prostate cancer radiation therapy. *J Med Imaging Radiat Oncol*. 2008;(January):419–424.

18. Tong X, Chen X, Li J, et al. Intrafractional prostate motion during external beam radiotherapy monitored by a real-time target localization system. *J Appl Clin Med Phys*. 2015;16(2):51–61.

19. Cramer AK, Haile AG, Ognjenovic S, et al. Real-time prostate motion assessment: image-guidance and the temporal dependence of intra-fraction motion. *BMC Med Phys*. 2013;13(1):4.

20. Li JS, Lin M-H, Buyyounouski MK, Horwitz EM, Ma C-M. Reduction of prostate intrafractional motion from shortening the treatment time. *Phys Med Biol*. 2013;58(14):4921–32..

21. Li R, Xing L. Bridging the gap between IMRT and VMAT: dense angularly sampled and sparse intensity modulated radiation therapy. *Med Phys*. 2011;38(9):4912–9.

22. Mittauer K, Lu B, Yan G, et al. A study of IMRT planning parameters on planning efficiency, delivery efficiency, and plan quality. *Med Phys*. 2013;40(6):061704.

23. Alvarez Moret J, Koelbl O, Bogner L. Quasi-IMAT technique and secondary cancer risk in prostate cancer. *Strahlenther Onkol*. 2009;185(4):248–53.

24. Murray L, Henry A, Hoskin P, Siebert F-A, Venselaar J. Second primary cancers after radiation for prostate cancer: a review of data from planning studies. *Radiat Oncol*. 2013;8:172.

25. Hussein M, Aldridge S, Guerrero Urbano T, Nisbet. The effect of 6 and 15 MV on intensity-modulated radiation therapy prostate cancer treatment: Plan evaluation, tumour control probability and normal tissue complication probability analysis, and the theoretical risk of secondary induced malignancies. *Br J Radiol*. 2012;85(April):423–432.

26. Chow JCL, Grigorov GN, Barnett RB. Study on surface dose generated in prostate intensity-modulated radiation therapy treatment. *Med Dosim*. 2006;31(4):249–58.

27. Mohan R, Arnfield M, Tong S, Wu Q, Siebers J. The impact of fluctuations in intensity patterns on the number of monitor units and the quality and accuracy of intensity modulated radiotherapy. *Med Phys*. 2000;27(6):1226–37.

28. Matuszak MM, Larsen EW, Fraass B. Reduction of IMRT beam complexity through the use of beam modulation penalties in the objective function. *Med Phys*. 2007;34(2):507.

29. Qi P, Xia P. Relationship of segment area and monitor unit efficiency in aperture-based IMRT optimization. In: *Journal of applied clinical medical physics / American College of Medical Physics*.Vol 14.; 2013:4056.

30. Takahashi Y, Koizumi M, Sumida I, et al. What is the Optimum Minimum Segment Size Used in Step and Shoot IMRT for Prostate Cancer? *J Radiat Res*. 2010;51(5):543–552.

31. Oliver M, Ansbacher W, Beckham W. Comparing planning time, delivery time and plan quality for IMRT, RapidArc and Tomotherapy. *J Appl Clin Med Phys*. 2009;10(4):3068.

32. Lu R, Radke RJ, Happersett L, et al. Reduced-order parameter optimization for simplifying prostate IMRT planning. *Phys Med Biol*. 2007;52(3):849–870.

33. Prabhakar R, Cramb J, Gehrke C, Anderson J, Andrews J. A study of segment weight optimization with the CMS XiO step-and-shoot IMRT technique for prostate cancer. *J Appl Clin Med Phys*. 2012.

34. Matuszak MM, Larsen EW, Jee K-W, McShan DL, Fraass B. Adaptive diffusion smoothing: A diffusion-based method to reduce IMRT field complexity. *Med Phys*. 2008;35(4):1532.

35. Sayre GA, Ruan D. Dose-shaping using targeted sparse optimization. *Med Phys*. 2013;90095(May):1–18.

36. Ehrgott M, Güler Ç, Hamacher HW, Shao L. Mathematical optimization in intensity modulated radiation therapy. *Ann Oper Res*. 2010;175:309–365.

37. Holdsworth C, Stewart RD, Kim M, Liao J, Phillips MH. Investigation of effective decision criteria for multiobjective optimization in IMRT. *Med Phys*. 2011;38(6):2964–2974.

38. Elekta. XiO IMRT Training Guide, version 4.63; section 9 pages 1- 30.

39. Grégoire V, Mackie TR. State of the art on dose prescription, reporting and recording in Intensity-Modulated Radiation Therapy (ICRU report No. 83). *Cancer Radiother*. 2011;15(6-7):555–9.

40. Olch AJ. Evaluation of the accuracy of 3DVH software estimates of dose to virtual ion chamber and film in composite IMRT QA. *Med Phys*. 2012;39(1):81–6.

41. Nelms BE, Chan MF, Jarry G, et al. Evaluating IMRT and VMAT dose accuracy: Practical examples of failure to detect systematic errors when applying a commonly used metric and action levels. *Med Phys*. 2013;40(11):111722.

42. Monti F, Ostinelli, Frigerio M, et al. An ICRU 50 radiotherapy treatment chart. *Radiother Oncol*. 1995;35(2):145–50.

43. Purdy J. Current ICRU definitions of volumes: limitations and future directions. *Semin Radiat Oncol*. 2004;14(1):27–40.

44. Jackson A, Marks LB, Bentzen SM et al. The lessons of QUANTEC: Recommendations for Reporting and Gathering Data on Dose-Volume Dependencies of Treatment Outcome. Int J Radiat Oncol Biol Phys 2010; 76(3 Suppl). *Semin Radiat Oncol*. 2013;23(3):155–6.

45. Becker L. *Statistical and Clinical Significance - Effect Size Calculators*.; 2016:4–7.

46. Yoon M, Park SY, Shin D, Lee SB. A new homogeneity index based on statistical analysis of the dose – volume histogram. *Spring*. 2007;8(2):9–17.

47. Das IJ. *Intensity Modulated Radiation Therapy ( IMRT ): Impact of ICRU 83*.; 2013:1–61.

48. Lim GJ, Holder A, Reese J. A clustering approach for optimizing beam angles in IMRT planning Mathematical Sciences Technical Report Series MSTR 09-03 A clustering approach for optimizing beam angles in IMRT planning. 2009;(812).

49. Waldron TJ. Functional Requirements for IMRT OR : Accelerator Fundamentals : Role and Impact on IMRT Accelerating Structures. In: *Functional Requirements for IMRT*. University of Texas, MD Anderson Cancer Center; :1–9.

50. http://www.healthcare.siemens.com/siemens_hwem-hwem_ssxa_websites-context-root/wcm/idc/groups/public/@global/@therapy/@radonco/documents/download/mdaw/mtyy/~edisp/siemens_160_mlc_datasheet-00094086.pdf. 160 MLC Multileaf Collimator.

51. Http://www.upscale.utoronto.ca/PVB/Harrison/ErrorAnalysis/. Error Analysis : An Introduction. :1–30.

52. Everitt, Brian S., Landau, Sabine, Leese, Morven, Stahl D. *Cluster Analysis*.; 2011:65–124.

53. Pao Y-H. *Statistical Pattern Recognition. Second edition (Keinosuke Fukunaga)*.; 1993:161–161.

54. Wang H, Wang W, et al. Clustering by pattern similarity in large data sets. *2002 ACM SIGMOD Int Conf Manag Data*. 2002;2:394.

55. Nelms BE, Zhen H, Tomé W. Per-beam, planar IMRT QA passing rates do not predict clinically relevant patient dose errors. *Med Phys*. 2011;38(2):1037.

56. Zhen H, Nelms BE, Tome W. Moving from gamma passing rates to patient DVH-based QA metrics in pretreatment dose QA. *Med Phys*. 2011;38(10):5477–89.

57. Hussein M, Rowshanfarzad P, Ebert M, Nisbet A, Clark CH. A comparison of the gamma index analysis in various commercial IMRT/VMAT QA systems. *Radiother Oncol*. 2013;109(3):370–6.

# Chapter 9

## 9 Appendix

### 9.1 Appendix A

#### 9.1.1 Data of the preliminary study

Table 9.1 indicates which optimization parameters had the biggest influence during the optimization process on MU's and segments for Patient X

*Table 9.1: Preliminary results of changing some optimization parameters for Patient X*

| **Patient X** | Min MU/segment | Segment size | Intensity level | Scatter Extent | Step Increment | Min. Transmission Multiplier | Smoothing parameter | Optimization margin | Total Segments | Total MU's | % Diff on Segments | % Diff on MU's |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Default | 5 | 2 | 7 | 1 | 2 | 1 | none | 0.5 | 60 | 492 | - | - |
| Plan 1 | 2 | 2 | 7 | 1 | 2 | 1 | none | 0.5 | 38 | 364 | 36.7 | 26.1 |
| Plan 2 | 10 | 2 | 7 | 1 | 2 | 1 | none | 0.5 | 26 | 360 | 56.7 | 26.9 |
| Plan 3 | 5 | 1 | 7 | 1 | 2 | 1 | none | 0.5 | 62 | 513 | 3.3 | 4.2 |
| Plan 4 | 5 | 3 | 7 | 1 | 2 | 1 | none | 0.5 | 51 | 454 | 15.0 | -7.8 |
| Plan 5 | 5 | 2 | 5 | 1 | 2 | 1 | none | 0.5 | 43 | 488 | 28.3 | -0.8 |
| Plan 6 | 5 | 2 | 7 | 1.5 | 2 | 1 | none | 0.5 | 58 | 479 | -3.3 | -2.8 |
| Plan 7 | 5 | 2 | 10 | 1 | 2 | 1 | none | 0.5 | 66 | 466 | 10.0 | -5.2 |
| Plan 8 | 5 | 2 | 7 | 1 | 1 | 1 | none | 0.5 | 67 | 711 | 11.7 | 44.5 |
| Plan 9 | 5 | 2 | 7 | 1 | 0.5 | 1 | none | 0.5 | 69 | 990 | 15.0 | 101.2 |
| Plan 10 | 5 | 2 | 7 | 1 | 2 | 2 | none | 0.5 | 58 | 492 | -3.3 | -0.1 |
| Plan 11 | 5 | 2 | 7 | 1 | 2 | 6 | none | 0.5 | 57 | 491 | -5.0 | -0.2 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Plan 12 | 5 | 2 | 7 | 1 | 2 | 1 | Complex Low | 0.5 | 59 | 493 | -1.7 | 0.1 |
| Plan 13 | 5 | 2 | 7 | 1 | 2 | 1 | Complex High | 0.5 | 60 | 487 | 0.0 | -1.0 |
| Plan 14 | 5 | 2 | 7 | 1 | 2 | 1 | General High | 0.5 | 49 | 414 | 18.3 | -15.9 |
| Plan 15 | 5 | 2 | 7 | 1 | 2 | 1 | Intermediate Low | 0.5 | 58 | 488 | -3.3 | -0.8 |
| Plan 16 | 5 | 2 | 7 | 1 | 2 | 1 | Intermediate High | 0.5 | 60 | 496 | 0.0 | 0.7 |
| Plan 17 | 5 | 2 | 7 | 1 | 2 | 1 | Simple Low | 0.5 | 57 | 474 | -5.0 | -3.7 |
| Plan 18 | 5 | 2 | 7 | 1 | 2 | 1 | Simple High | 0.5 | 57 | 427 | -5.0 | -13.3 |
| Plan 19 | 5 | 2 | 7 | 1 | 2 | 1 | none | 1 | 64 | 521 | 6.7 | 5.9 |

## 9.2 Appendix B

### 9.2.1 An example calculation of the HI and CI for Patient A

HI (Eq. 2) and CI (Eq. 3) are calculated for Patient A (PTV 1); all values were obtained from the TPS as indicated by, calculation shown is for the default plan (Plan no.1).

$$\mathrm{HI} = \frac{\mathrm{D_2} - \mathrm{D_{98}}}{\mathrm{D_p}} = \frac{7365 - 6362}{7000} = 0.143 \quad (2)$$

$$\mathrm{CI} = \frac{\mathrm{TV}}{\mathrm{PTV}} = \frac{59.92}{71.15} = 0.842 \quad (3)$$

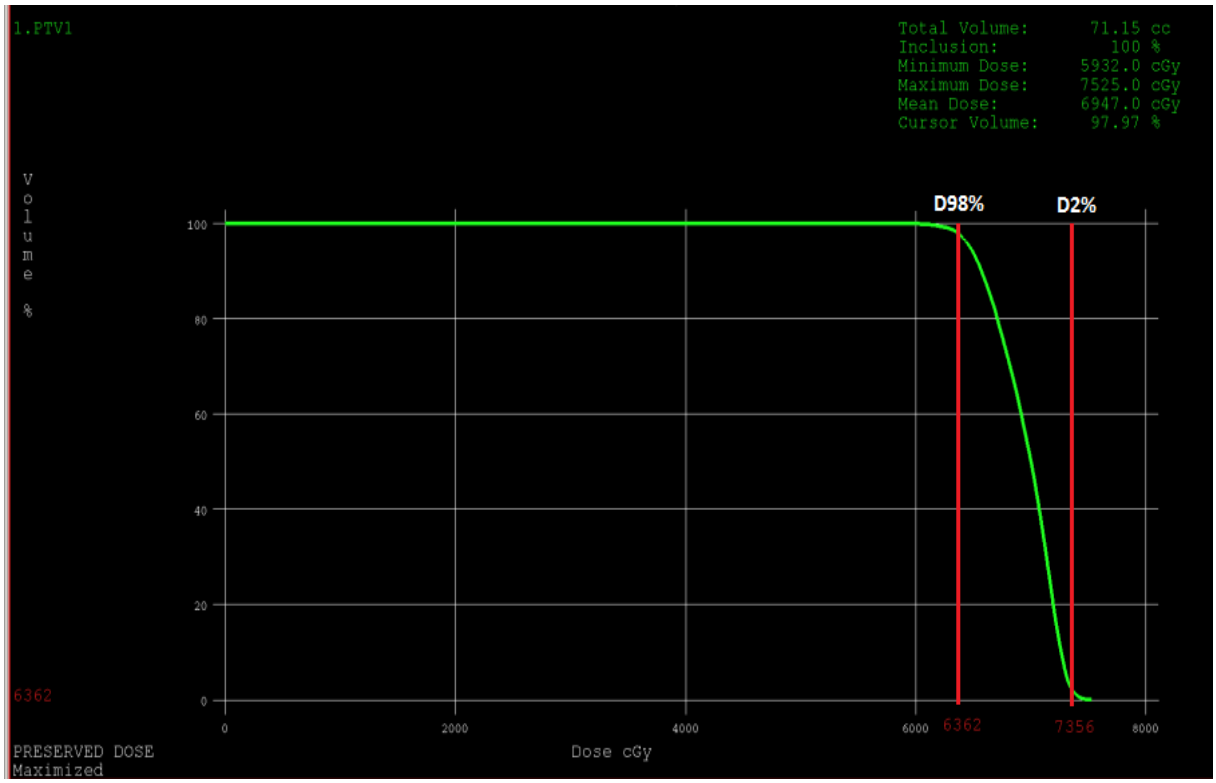



*Figure 9.1: Illustration of the $D_{98}$ and $D_2$ values which was obtained from the DVH of Patient A, plan no 1, to calculate HI.*

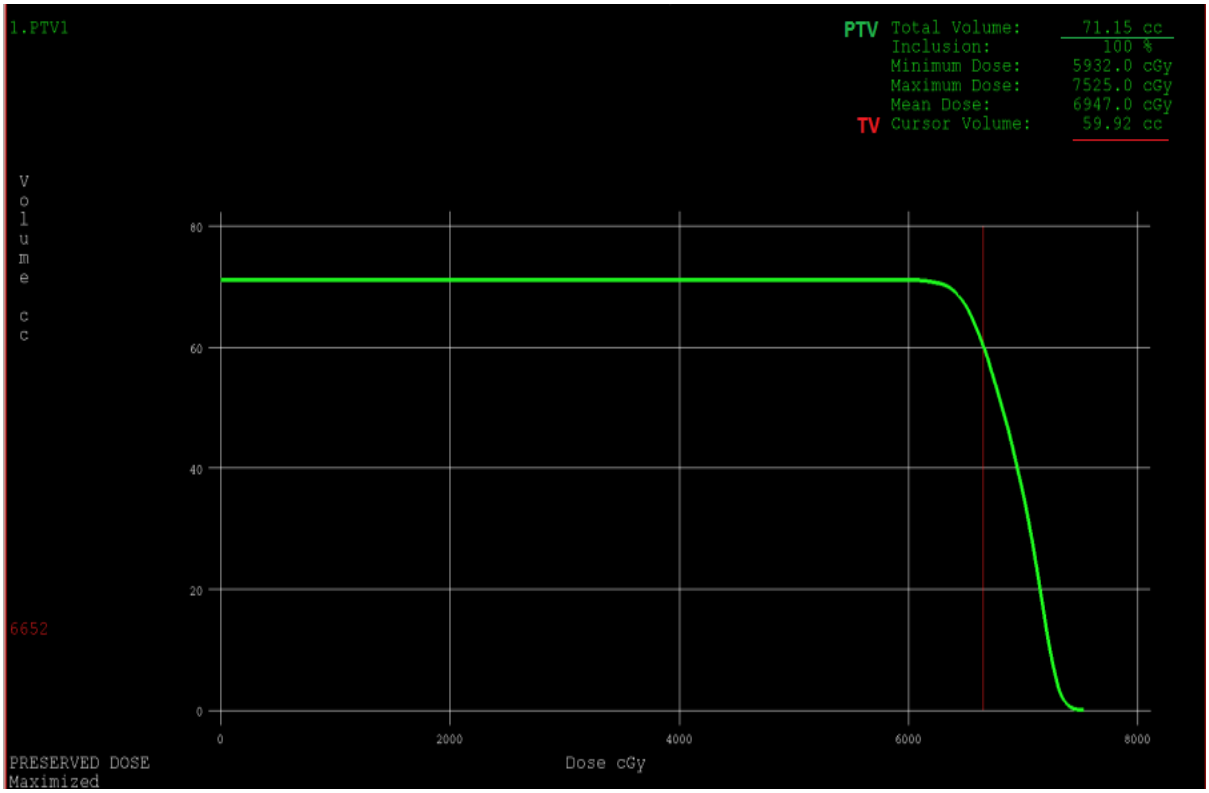



*Figure 9.2: Illustration of the volume sizes obtained from the DVH for TV (volume receiving 95% of the prescribed dose) and PTV, for Patient A, plan no 1, to calculated CI*

## 9.3 Appendix C

### 9.3.1 A calculation of the delivery time and the error for Patient 1

An example calculation of the delivery time and the error for Patient 1 using Eq. 4 and 5 from Chapter 4.

Details of Patient 1: 7 fields, 15 MV, 637 MU, 82 Segments, 16 cm average field size, obtained from the TPS.

All other components (Machine input values), needed for calculation was obtained from Table 4.2

**Calculated delivery time (T) for Patient 1:**

$$T=\frac{MU}{DR}+\left[T_G \times \left(1-\frac{1}{N_B}\right)\right]+\left[\Delta T_G \times (N_B-1)\right]+[RF \times (N_B)]+T_{MLC} \quad (4)$$

$$T_{MLC}=\frac{(FS \times N_B)}{MLC_{speed}}+\left[MLC_{delay} \times (N_s-(N_B-1))\right] \quad (5)$$

$$T=\left[\frac{637\ MU}{8.88\ MU.s^{-1}}\right]+\left[81.8\ s \times \left(1-\frac{1}{7}\right)\right]+[6.6\ s \times (7-1)]+[3\ s \times 7]$$
$$+\left\{\left(\frac{16\ cm \times 7}{1.3\ cm.s^{-1}}\right)+[2.5\ s \times (82-(7-1))]\right\}$$

$$T=71.73\ s+70.10\ s+39.6\ s+21\ s+86.15\ s+190\ s=\mathbf{479\ s=7.58}\ \text{min}$$

**Error calculated ($\delta T$) for Patient 1 (Absolute errors were obtain from Table 4.2):**[51]

$$\delta T=\sqrt{\left[\sqrt{\left(\frac{\delta DR}{DR}\right)^2}\ x\ \left(\frac{MU}{DR}\right)\right]^2+\left[\delta T_G\ x\ \left(1-\frac{1}{N_B}\right)\right]^2+[\delta \Delta T_G\ x\ (N_B-1)]^2+[\delta RF\ x\ N_B]^2+\left[\left(\frac{FS\ x\ N_B}{MLC_{speed}}\right)\ x\ \sqrt{\left(\frac{\delta MLC_{speed}}{MLC_{speed}}\right)^2}\right]+\left[\delta MLC_{delay}\ x\ \left(N_s-(N_B-1)\right)\right]^2}$$

$$=\sqrt{\left[\sqrt{\left(\frac{0.03\ MUs^{-1}}{8.88\ MUs^{-1}}\right)^2}\ x\ \left(\frac{637\ MU}{8.88\ MUs^{-1}}\right)\right]^2+\left[0.2\ s\ x\ \left(1-\frac{1}{7}\right)\right]^2+[0.6\ s\ x\ (7-1)]^2+[0.4\ s\ x\ 7]^2+\left[\left(\frac{16\ cm\ x\ 7}{1.31\ cms^{-1}}\right)\ x\ \sqrt{\left(\frac{0.1\ cms^{-1}}{1.31\ cms^{-1}}\right)^2}\right]+\left[0.1\ s\ x\ \left(82-(7-1)\right)\right]^2}$$

$$\delta T=\sqrt{[0.27\ s]^2+[0.17\ s]^2+[3.6\ s]^2+[2.8\ s]^2+[6.58\ s]^2+[7.6\ s]^2}$$

$$\delta T=\mathbf{11\ s}$$

## 9.4 Appendix D

### 9.4.1 The tabulated results of the five variables calculated and normalized to the default (plan no. 1) for all 15 patients (both energies).

| Patient A – 15 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.00 | 1.09 | 0.94 | 1.03 | 1.03 |
| 3 | 0.98 | 0.76 | 1.06 | 1.06 | 0.90 |
| 4 | 1.08 | 0.84 | 0.92 | 1.02 | 0.95 |
| 5 | 0.97 | 1.13 | 0.98 | 1.05 | 1.05 |
| 6 | 0.90 | 0.79 | 1.01 | 1.03 | 0.90 |
| 7 | 0.80 | 0.85 | 1.09 | 0.97 | 0.91 |
| 8 | 0.97 | 1.01 | 0.96 | 1.02 | 1.00 |
| 9 | 0.91 | 0.93 | 0.99 | 1.02 | 0.96 |
| 10 | 0.80 | 1.41 | 0.95 | 1.07 | 1.13 |
| 11 | 0.92 | 0.51 | 1.19 | 1.08 | 0.80 |
| 12 | 0.79 | 0.65 | 1.04 | 1.05 | 0.83 |
| 13 | 0.88 | 0.81 | 1.04 | 1.04 | 0.91 |
| 14 | 0.86 | 0.79 | 1.04 | 1.04 | 0.90 |
| 15 | 0.76 | 0.71 | 1.03 | 1.07 | 0.85 |
| 16 | 0.80 | 0.74 | 1.06 | 1.05 | 0.86 |

| Patient A – 6 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.14 | 1.10 | 0.96 | 1.05 | 1.06 |
| 3 | 1.14 | 0.79 | 1.09 | 1.08 | 0.94 |
| 4 | 1.20 | 0.84 | 0.91 | 1.06 | 0.97 |
| 5 | 1.09 | 1.24 | 1.04 | 1.06 | 1.11 |
| 6 | 1.06 | 0.90 | 1.03 | 1.04 | 0.97 |
| 7 | 0.92 | 0.88 | 1.06 | 1.00 | 0.94 |
| 8 | 1.10 | 1.01 | 0.98 | 1.04 | 1.02 |
| 9 | 1.08 | 0.94 | 1.11 | 0.98 | 0.99 |
| 10 | 0.82 | 0.91 | 0.99 | 1.09 | 0.94 |
| 11 | 1.00 | 0.50 | 1.19 | 1.09 | 0.81 |
| 12 | 0.84 | 0.75 | 1.09 | 1.08 | 0.88 |
| 13 | 0.91 | 0.87 | 1.09 | 1.06 | 0.93 |
| 14 | 0.91 | 0.85 | 1.08 | 1.06 | 0.93 |
| 15 | 0.88 | 0.81 | 1.04 | 1.09 | 0.91 |
| 16 | 0.85 | 0.75 | 0.97 | 1.08 | 0.88 |

| Patient B – 15 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.03 | 1.02 | 0.88 | 1.02 | 1.02 |
| 3 | 1.03 | 0.94 | 0.97 | 1.02 | 0.98 |
| 4 | 1.10 | 0.80 | 0.89 | 1.02 | 0.94 |
| 5 | 0.98 | 1.29 | 0.93 | 1.01 | 1.12 |
| 6 | 0.91 | 0.81 | 1.13 | 1.00 | 0.90 |
| 7 | 0.76 | 0.87 | 0.84 | 1.00 | 0.90 |
| 8 | 0.89 | 0.97 | 0.86 | 1.02 | 0.96 |
| 9 | 0.93 | 0.94 | 0.88 | 1.00 | 0.97 |
| 10 | 0.80 | 1.94 | 0.97 | 1.00 | 1.36 |
| 11 | 0.74 | 0.53 | 1.12 | 0.98 | 0.75 |
| 12 | 0.74 | 0.82 | 1.08 | 1.01 | 0.87 |
| 13 | 0.76 | 0.87 | 1.04 | 1.00 | 0.90 |
| 14 | 0.76 | 0.87 | 1.04 | 1.00 | 0.90 |
| 15 | 0.70 | 0.78 | 1.04 | 1.00 | 0.85 |
| 16 | 0.74 | 0.89 | 1.00 | 0.97 | 0.90 |

| Patient B– 6 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.05 | 0.96 | 0.85 | 1.03 | 0.99 |
| 3 | 1.04 | 0.86 | 0.89 | 1.02 | 0.95 |
| 4 | 1.14 | 0.76 | 0.93 | 1.01 | 0.92 |
| 5 | 1.00 | 1.26 | 0.84 | 1.02 | 1.11 |
| 6 | 0.97 | 0.79 | 1.09 | 1.01 | 0.90 |
| 7 | 0.88 | 0.90 | 0.82 | 1.00 | 0.93 |
| 8 | 1.00 | 0.96 | 0.83 | 1.01 | 0.98 |
| 9 | 0.92 | 0.92 | 0.83 | 1.01 | 0.95 |
| 10 | 0.82 | 1.91 | 0.92 | 1.00 | 1.35 |
| 11 | 0.70 | 0.52 | 1.06 | 0.97 | 0.74 |
| 12 | 0.73 | 0.81 | 1.03 | 1.02 | 0.87 |
| 13 | 0.80 | 0.90 | 0.99 | 0.99 | 0.92 |
| 14 | 0.80 | 0.90 | 1.01 | 0.99 | 0.92 |
| 15 | 0.78 | 0.83 | 0.98 | 0.99 | 0.89 |
| 16 | 0.77 | 0.88 | 0.96 | 0.99 | 0.90 |

| Patient C – 15 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 0.93 | 0.96 | 0.80 | 0.99 | 0.98 |
| 3 | 0.87 | 0.68 | 0.83 | 1.00 | 0.86 |
| 4 | 0.94 | 0.70 | 0.93 | 1.01 | 0.88 |
| 5 | 0.85 | 1.08 | 0.92 | 1.02 | 1.01 |
| 6 | 0.89 | 0.92 | 0.82 | 1.00 | 0.96 |
| 7 | 0.78 | 0.70 | 0.83 | 1.02 | 0.86 |
| 8 | 0.92 | 0.94 | 0.91 | 1.00 | 0.97 |
| 9 | 0.85 | 0.91 | 0.86 | 1.01 | 0.95 |
| 10 | 0.73 | 0.53 | 0.84 | 1.02 | 0.79 |
| 11 | 0.83 | 0.38 | 1.00 | 1.03 | 0.75 |
| 12 | 0.79 | 0.51 | 0.84 | 1.03 | 0.79 |
| 13 | 0.78 | 0.49 | 0.89 | 1.02 | 0.78 |
| 14 | 0.78 | 0.49 | 0.88 | 1.02 | 0.78 |
| 15 | 0.78 | 0.47 | 0.82 | 1.04 | 0.77 |
| 16 | 0.75 | 0.40 | 0.76 | 1.03 | 0.74 |

| Patient C – 6 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.02 | 0.94 | 0.82 | 1.00 | 0.98 |
| 3 | 0.96 | 0.72 | 0.94 | 0.99 | 0.89 |
| 4 | 1.03 | 0.68 | 0.87 | 1.00 | 0.88 |
| 5 | 0.97 | 1.15 | 0.86 | 1.03 | 1.05 |
| 6 | 0.89 | 0.92 | 0.81 | 1.00 | 0.96 |
| 7 | 0.88 | 0.74 | 0.79 | 1.02 | 0.89 |
| 8 | 1.02 | 0.92 | 0.84 | 1.01 | 0.97 |
| 9 | 0.93 | 0.85 | 0.83 | 1.03 | 0.93 |
| 10 | 0.91 | 1.09 | 0.86 | 1.02 | 1.03 |
| 11 | 0.89 | 0.34 | 0.94 | 1.01 | 0.74 |
| 12 | 0.86 | 0.51 | 0.78 | 1.03 | 0.80 |
| 13 | 0.97 | 0.60 | 0.83 | 1.03 | 0.85 |
| 14 | 0.97 | 0.60 | 0.84 | 1.03 | 0.85 |
| 15 | 0.89 | 0.55 | 0.75 | 1.03 | 0.82 |
| 16 | 0.80 | 0.40 | 0.60 | 1.05 | 0.75 |

| Patient D – 15 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.04 | 1.03 | 0.88 | 1.02 | 1.02 |
| 3 | 1.00 | 0.69 | 1.21 | 1.01 | 0.88 |
| 4 | 1.11 | 0.80 | 0.91 | 1.01 | 0.93 |
| 5 | 1.00 | 1.14 | 1.16 | 1.00 | 1.05 |
| 6 | 0.94 | 0.78 | 1.05 | 1.01 | 0.90 |
| 7 | 0.82 | 0.80 | 1.10 | 1.01 | 0.89 |
| 8 | 0.98 | 0.95 | 1.05 | 1.02 | 0.98 |
| 9 | 0.88 | 0.89 | 1.05 | 1.01 | 0.94 |
| 10 | 0.79 | 0.72 | 1.05 | 1.00 | 0.86 |
| 11 | 0.78 | 0.34 | 1.16 | 0.99 | 0.70 |
| 12 | 0.84 | 0.49 | 1.07 | 1.01 | 0.77 |
| 13 | 0.85 | 0.58 | 1.07 | 1.01 | 0.81 |
| 14 | 0.85 | 0.58 | 1.06 | 1.01 | 0.81 |
| 15 | 0.78 | 0.54 | 1.17 | 1.00 | 0.78 |
| 16 | 0.71 | 0.48 | 1.20 | 0.99 | 0.75 |

| Patient D – 6 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.20 | 1.02 | 0.94 | 1.00 | 1.03 |
| 3 | 1.00 | 0.69 | 1.22 | 1.01 | 0.88 |
| 4 | 1.30 | 0.78 | 0.88 | 1.01 | 0.96 |
| 5 | 1.21 | 1.23 | 1.03 | 1.00 | 1.12 |
| 6 | 1.17 | 0.86 | 1.12 | 1.00 | 0.97 |
| 7 | 1.02 | 0.95 | 0.94 | 1.01 | 0.98 |
| 8 | 1.20 | 1.02 | 0.95 | 1.00 | 1.03 |
| 9 | 1.05 | 0.95 | 0.98 | 1.01 | 0.99 |
| 10 | 1.00 | 1.03 | 1.05 | 1.00 | 1.01 |
| 11 | 0.94 | 0.42 | 1.17 | 0.97 | 0.75 |
| 12 | 0.93 | 0.51 | 1.16 | 0.98 | 0.79 |
| 13 | 0.96 | 0.60 | 1.18 | 0.98 | 0.83 |
| 14 | 0.96 | 0.58 | 1.16 | 0.98 | 0.83 |
| 15 | 0.87 | 0.62 | 1.17 | 0.97 | 0.82 |
| 16 | 0.86 | 0.55 | 1.21 | 0.98 | 0.80 |

| Patient E– 15 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.03 | 1.03 | 0.85 | 0.94 | 1.02 |
| 3 | 1.01 | 0.86 | 0.97 | 1.03 | 0.94 |
| 4 | 1.11 | 0.80 | 1.12 | 0.99 | 0.93 |
| 5 | 1.00 | 1.25 | 1.15 | 0.96 | 1.10 |
| 6 | 0.96 | 0.89 | 0.99 | 0.99 | 0.95 |
| 7 | 0.94 | 0.97 | 0.90 | 0.92 | 0.98 |
| 8 | 1.04 | 1.05 | 0.86 | 0.94 | 1.03 |
| 9 | 0.95 | 0.97 | 0.88 | 0.94 | 0.98 |
| 10 | 0.80 | 0.84 | 0.94 | 0.98 | 0.91 |
| 11 | 0.78 | 0.48 | 1.19 | 1.02 | 0.76 |
| 12 | 0.86 | 0.66 | 1.24 | 0.97 | 0.84 |
| 13 | 0.91 | 0.80 | 1.24 | 0.96 | 0.90 |
| 14 | 0.92 | 0.81 | 1.24 | 0.96 | 0.91 |
| 15 | 0.92 | 0.75 | 1.02 | 1.03 | 0.89 |
| 16 | 0.85 | 0.67 | 1.05 | 1.00 | 0.84 |

| Patient E – 6 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.20 | 1.02 | 0.94 | 1.00 | 1.03 |
| 3 | 1.00 | 0.69 | 1.22 | 1.01 | 0.88 |
| 4 | 1.30 | 0.78 | 0.88 | 1.01 | 0.96 |
| 5 | 1.21 | 1.23 | 1.03 | 1.00 | 1.12 |
| 6 | 1.17 | 0.86 | 1.12 | 1.00 | 0.97 |
| 7 | 1.02 | 0.95 | 0.94 | 1.01 | 0.98 |
| 8 | 1.20 | 1.02 | 0.95 | 1.00 | 1.03 |
| 9 | 1.05 | 0.95 | 0.98 | 1.01 | 0.99 |
| 10 | 1.00 | 1.03 | 1.05 | 1.00 | 1.01 |
| 11 | 0.94 | 0.42 | 1.17 | 0.97 | 0.75 |
| 12 | 0.93 | 0.51 | 1.16 | 0.98 | 0.79 |
| 13 | 0.96 | 0.60 | 1.18 | 0.98 | 0.83 |
| 14 | 0.96 | 0.58 | 1.16 | 0.98 | 0.83 |
| 15 | 0.87 | 0.62 | 1.17 | 0.97 | 0.82 |
| 16 | 0.86 | 0.55 | 1.21 | 0.98 | 0.80 |

| Patient F – 15 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 0.76 | 1.06 | 0.80 | 0.93 | 0.97 |
| 3 | 0.76 | 0.95 | 0.97 | 0.93 | 0.93 |
| 4 | 0.81 | 0.81 | 0.84 | 1.00 | 0.89 |
| 5 | 0.75 | 1.39 | 0.85 | 0.97 | 1.09 |
| 6 | 0.71 | 0.90 | 0.96 | 1.00 | 0.90 |
| 7 | 0.63 | 0.96 | 0.79 | 0.97 | 0.91 |
| 8 | 0.75 | 1.04 | 0.80 | 0.98 | 0.96 |
| 9 | 0.75 | 1.04 | 0.80 | 0.88 | 0.96 |
| 10 | 0.65 | 1.84 | 0.89 | 1.01 | 1.24 |
| 11 | 0.62 | 0.64 | 0.90 | 0.94 | 0.79 |
| 12 | 0.57 | 0.84 | 0.88 | 0.94 | 0.85 |
| 13 | 0.60 | 0.90 | 0.87 | 0.93 | 0.88 |
| 14 | 0.60 | 0.90 | 0.87 | 0.99 | 0.88 |
| 15 | 0.61 | 0.90 | 0.88 | 0.96 | 0.88 |
| 16 | 0.57 | 0.79 | 0.90 | 1.00 | 0.83 |

| Patient F – 6 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 0.78 | 1.04 | 0.76 | 0.91 | 0.97 |
| 3 | 0.76 | 0.87 | 0.88 | 0.90 | 0.90 |
| 4 | 0.83 | 0.78 | 0.87 | 0.97 | 0.88 |
| 5 | 0.78 | 1.42 | 0.78 | 0.95 | 1.11 |
| 6 | 0.75 | 0.92 | 0.80 | 1.01 | 0.92 |
| 7 | 0.64 | 0.92 | 0.75 | 0.90 | 0.90 |
| 8 | 0.79 | 1.01 | 0.77 | 0.93 | 0.96 |
| 9 | 0.74 | 0.99 | 0.76 | 0.87 | 0.94 |
| 10 | 0.68 | 1.97 | 0.81 | 0.92 | 1.24 |
| 11 | 0.18 | 0.16 | 0.94 | 0.55 | 0.51 |
| 12 | 0.60 | 0.83 | 0.89 | 0.97 | 0.85 |
| 13 | 0.64 | 0.96 | 0.90 | 0.95 | 0.91 |
| 14 | 0.21 | 0.30 | 0.87 | 0.46 | 0.57 |
| 15 | 0.64 | 0.92 | 0.85 | 1.01 | 0.89 |
| 16 | 0.58 | 0.79 | 0.84 | 0.88 | 0.83 |

| Patient G – 15 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 0.98 | 1.00 | 0.87 | 1.36 | 1.00 |
| 3 | 0.97 | 0.72 | 0.99 | 1.36 | 0.88 |
| 4 | 1.00 | 0.69 | 0.85 | 1.06 | 0.87 |
| 5 | 0.92 | 1.06 | 1.01 | 1.06 | 1.01 |
| 6 | 0.92 | 0.85 | 0.92 | 1.06 | 0.92 |
| 7 | 0.83 | 0.85 | 0.89 | 1.07 | 0.91 |
| 8 | 0.98 | 0.93 | 0.95 | 1.04 | 0.97 |
| 9 | 0.92 | 0.90 | 0.92 | 1.07 | 0.95 |
| 10 | 0.85 | 1.33 | 0.96 | 1.06 | 1.12 |
| 11 | 0.66 | 0.36 | 1.22 | 0.99 | 0.67 |
| 12 | 0.75 | 0.61 | 1.10 | 1.05 | 0.79 |
| 13 | 0.79 | 0.67 | 1.13 | 1.04 | 0.82 |
| 14 | 0.79 | 0.67 | 1.13 | 1.04 | 0.82 |
| 15 | 0.81 | 0.72 | 1.07 | 1.03 | 0.85 |
| 16 | 0.76 | 0.60 | 1.08 | 1.06 | 0.79 |

| Patient G – 6 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.06 | 0.96 | 0.88 | 1.07 | 0.99 |
| 3 | 1.03 | 0.72 | 0.98 | 1.08 | 0.89 |
| 4 | 1.13 | 0.75 | 0.88 | 1.05 | 0.98 |
| 5 | 1.04 | 1.14 | 0.87 | 1.07 | 0.97 |
| 6 | 1.00 | 0.76 | 0.93 | 1.07 | 0.90 |
| 7 | 0.95 | 0.88 | 0.85 | 1.07 | 0.96 |
| 8 | 1.03 | 0.89 | 0.83 | 1.04 | 0.95 |
| 9 | 0.96 | 0.83 | 0.80 | 1.06 | 0.92 |
| 10 | 0.90 | 1.51 | 0.96 | 1.06 | 0.94 |
| 11 | 0.75 | 0.42 | 1.29 | 1.00 | 0.93 |
| 12 | 0.78 | 0.60 | 1.07 | 1.04 | 0.79 |
| 13 | 0.83 | 0.68 | 1.13 | 1.04 | 0.92 |
| 14 | 0.84 | 0.65 | 1.13 | 1.04 | 0.91 |
| 15 | 0.80 | 0.61 | 1.13 | 1.04 | 0.80 |
| 16 | 0.86 | 0.76 | 1.00 | 1.06 | 0.91 |

| Patient H – 15 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.01 | 1.01 | 0.93 | 0.88 | 1.01 |
| 3 | 0.95 | 0.67 | 1.19 | 0.98 | 0.85 |
| 4 | 1.08 | 0.78 | 0.99 | 0.93 | 0.91 |
| 5 | 0.94 | 1.06 | 0.98 | 0.93 | 1.02 |
| 6 | 0.91 | 0.81 | 0.93 | 0.91 | 0.90 |
| 7 | 0.84 | 0.88 | 1.01 | 0.85 | 0.93 |
| 8 | 1.23 | 1.08 | 1.00 | 0.97 | 1.07 |
| 9 | 1.04 | 0.95 | 1.00 | 0.98 | 0.98 |
| 10 | 0.82 | 1.12 | 1.10 | 0.96 | 1.03 |
| 11 | 0.68 | 0.33 | 1.22 | 0.94 | 0.66 |
| 12 | 0.71 | 0.42 | 1.17 | 0.93 | 0.70 |
| 13 | 0.74 | 0.49 | 1.12 | 0.93 | 0.74 |
| 14 | 0.74 | 0.49 | 1.13 | 0.95 | 0.74 |
| 15 | 0.71 | 0.45 | 1.13 | 0.93 | 0.71 |
| 16 | 0.72 | 0.54 | 1.16 | 0.87 | 0.75 |

| Patient H – 6 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.12 | 0.99 | 1.12 | 0.99 | 1.01 |
| 3 | 1.11 | 0.72 | 1.39 | 0.93 | 0.89 |
| 4 | 1.21 | 0.77 | 1.06 | 0.96 | 0.93 |
| 5 | 1.05 | 1.13 | 1.16 | 0.94 | 1.07 |
| 6 | 1.02 | 0.83 | 1.23 | 0.96 | 0.93 |
| 7 | 0.93 | 0.88 | 0.97 | 0.86 | 0.94 |
| 8 | 1.33 | 1.06 | 1.16 | 0.97 | 1.08 |
| 9 | 1.16 | 0.97 | 1.22 | 0.99 | 1.01 |
| 10 | 0.91 | 1.22 | 1.21 | 0.97 | 1.08 |
| 11 | 0.71 | 0.31 | 1.44 | 0.92 | 0.65 |
| 12 | 0.77 | 0.51 | 1.32 | 0.93 | 0.75 |
| 13 | 0.80 | 0.59 | 1.32 | 0.96 | 0.79 |
| 14 | 0.80 | 0.59 | 1.30 | 0.94 | 0.79 |
| 15 | 0.79 | 0.53 | 1.30 | 0.93 | 0.76 |
| 16 | 0.81 | 0.46 | 1.35 | 1.00 | 0.73 |

| Patient I – 15 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 0.99 | 1.00 | 0.93 | 0.99 | 1.00 |
| 3 | 0.99 | 0.78 | 1.19 | 1.00 | 0.91 |
| 4 | 1.06 | 0.79 | 0.99 | 0.97 | 0.92 |
| 5 | 1.03 | 1.28 | 0.98 | 1.00 | 1.12 |
| 6 | 0.96 | 0.90 | 0.93 | 1.00 | 0.95 |
| 7 | 0.92 | 0.96 | 1.01 | 0.97 | 0.97 |
| 8 | 1.04 | 1.04 | 1.00 | 1.00 | 1.02 |
| 9 | 1.04 | 1.04 | 1.00 | 1.01 | 1.02 |
| 10 | 0.85 | 1.36 | 1.10 | 0.98 | 1.12 |
| 11 | 0.68 | 0.39 | 1.22 | 0.89 | 0.70 |
| 12 | 0.77 | 0.61 | 1.17 | 0.95 | 0.80 |
| 13 | 0.76 | 0.76 | 1.12 | 0.96 | 0.86 |
| 14 | 0.76 | 0.72 | 1.13 | 0.96 | 0.85 |
| 15 | 0.80 | 0.72 | 1.13 | 0.94 | 0.85 |
| 16 | 0.78 | 0.60 | 1.16 | 0.94 | 0.80 |

| Patient I – 6 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.18 | 1.06 | 1.05 | 0.98 | 1.05 |
| 3 | 1.19 | 0.89 | 1.07 | 1.01 | 0.99 |
| 4 | 1.23 | 0.79 | 1.03 | 0.98 | 0.95 |
| 5 | 1.13 | 1.28 | 1.02 | 1.00 | 1.13 |
| 6 | 1.12 | 0.93 | 1.01 | 0.99 | 0.99 |
| 7 | 1.03 | 0.90 | 1.08 | 0.95 | 0.97 |
| 8 | 1.25 | 1.08 | 1.03 | 1.00 | 1.08 |
| 9 | 1.16 | 1.06 | 1.11 | 0.97 | 1.05 |
| 10 | 0.99 | 1.51 | 1.25 | 1.00 | 1.21 |
| 11 | 0.84 | 0.50 | 1.13 | 0.93 | 0.77 |
| 12 | 0.86 | 0.64 | 1.08 | 0.96 | 0.83 |
| 13 | 0.89 | 0.82 | 1.07 | 0.95 | 0.91 |
| 14 | 0.89 | 0.79 | 1.14 | 0.95 | 0.90 |
| 15 | 0.90 | 0.83 | 1.19 | 0.99 | 0.91 |
| 16 | 0.87 | 0.69 | 1.04 | 0.98 | 0.85 |

| Patient J – 15 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.05 | 1.00 | 1.02 | 0.69 | 1.01 |
| 3 | 1.04 | 0.68 | 1.19 | 1.16 | 0.87 |
| 4 | 1.03 | 0.70 | 0.98 | 0.67 | 0.88 |
| 5 | 1.01 | 1.05 | 1.10 | 1.18 | 1.03 |
| 6 | 0.99 | 0.86 | 1.08 | 1.18 | 0.94 |
| 7 | 0.92 | 0.85 | 1.10 | 1.15 | 0.92 |
| 8 | 1.04 | 0.91 | 1.07 | 1.18 | 0.97 |
| 9 | 1.02 | 0.92 | 1.10 | 0.69 | 0.97 |
| 10 | 0.66 | 0.81 | 1.35 | 1.10 | 0.87 |
| 11 | 0.68 | 0.27 | 1.31 | 0.99 | 0.64 |
| 12 | 0.64 | 0.42 | 1.45 | 1.03 | 0.70 |
| 13 | 0.58 | 0.38 | 1.49 | 1.00 | 0.67 |
| 14 | 0.58 | 0.38 | 1.48 | 1.00 | 0.67 |
| 15 | 0.68 | 0.49 | 1.42 | 1.02 | 0.73 |
| 16 | 0.61 | 0.36 | 1.56 | 0.62 | 0.67 |

| Patient J – 6 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.20 | 1.01 | 1.04 | 1.17 | 1.03 |
| 3 | 1.18 | 0.76 | 1.21 | 1.17 | 0.92 |
| 4 | 1.23 | 0.74 | 1.03 | 1.16 | 0.92 |
| 5 | 1.15 | 1.18 | 1.11 | 1.17 | 1.10 |
| 6 | 1.13 | 0.84 | 1.15 | 1.14 | 0.95 |
| 7 | 1.01 | 0.84 | 1.05 | 1.16 | 0.93 |
| 8 | 1.14 | 0.95 | 1.03 | 1.18 | 1.00 |
| 9 | 1.13 | 0.91 | 1.00 | 1.20 | 0.98 |
| 10 | 0.72 | 0.34 | 1.50 | 1.02 | 0.68 |
| 11 | 0.69 | 0.27 | 0.77 | 0.99 | 0.64 |
| 12 | 0.77 | 0.39 | 1.40 | 1.14 | 0.71 |
| 13 | 0.75 | 0.49 | 1.48 | 1.10 | 0.74 |
| 14 | 0.75 | 0.45 | 1.44 | 1.10 | 0.73 |
| 15 | 0.74 | 0.49 | 1.51 | 1.09 | 0.74 |
| 16 | 0.72 | 0.42 | 1.53 | 1.12 | 0.71 |

| Patient K – 15 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.02 | 1.01 | 0.90 | 1.00 | 1.01 |
| 3 | 1.03 | 0.88 | 1.01 | 0.97 | 0.95 |
| 4 | 1.09 | 0.78 | 0.94 | 0.98 | 0.93 |
| 5 | 1.01 | 1.35 | 0.87 | 1.01 | 1.14 |
| 6 | 1.08 | 0.88 | 0.97 | 0.99 | 0.97 |
| 7 | 0.93 | 0.99 | 0.85 | 0.98 | 0.98 |
| 8 | 1.00 | 0.99 | 0.41 | 0.99 | 1.00 |
| 9 | 1.02 | 1.01 | 0.88 | 0.99 | 1.01 |
| 10 | 0.81 | 1.89 | 0.97 | 0.99 | 1.32 |
| 11 | 0.75 | 0.57 | 0.96 | 0.99 | 0.78 |
| 12 | 0.74 | 0.82 | 0.98 | 0.98 | 0.88 |
| 13 | 0.79 | 0.90 | 0.98 | 0.99 | 0.93 |
| 14 | 0.79 | 0.90 | 0.97 | 0.99 | 0.93 |
| 15 | 0.78 | 0.85 | 0.96 | 0.98 | 0.90 |
| 16 | 0.79 | 0.96 | 1.00 | 0.86 | 0.95 |

| Patient K – 6 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.19 | 1.04 | 0.84 | 0.99 | 1.05 |
| 3 | 1.19 | 0.99 | 0.89 | 0.99 | 1.03 |
| 4 | 1.26 | 0.79 | 0.92 | 0.99 | 0.96 |
| 5 | 1.10 | 1.29 | 0.85 | 1.01 | 1.13 |
| 6 | 1.08 | 0.88 | 0.97 | 0.99 | 0.97 |
| 7 | 1.02 | 0.94 | 0.82 | 0.98 | 0.98 |
| 8 | 1.14 | 1.00 | 0.84 | 0.99 | 1.03 |
| 9 | 1.14 | 1.00 | 0.82 | 1.00 | 1.02 |
| 10 | 0.92 | 2.07 | 0.93 | 0.99 | 1.41 |
| 11 | 0.78 | 0.56 | 1.02 | 0.99 | 0.78 |
| 12 | 0.88 | 1.00 | 0.95 | 0.98 | 0.98 |
| 13 | 0.90 | 1.00 | 0.94 | 0.98 | 0.98 |
| 14 | 0.89 | 0.97 | 0.94 | 0.98 | 0.97 |
| 15 | 0.88 | 0.97 | 0.91 | 0.99 | 0.97 |
| 16 | 0.85 | 0.94 | 0.90 | 0.99 | 0.95 |

| Patient L – 15 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 0.90 | 0.90 | 0.93 | 1.03 | 0.94 |
| 3 | 0.87 | 0.65 | 1.19 | 1.01 | 0.82 |
| 4 | 0.91 | 0.66 | 0.99 | 1.02 | 0.83 |
| 5 | 0.88 | 1.04 | 0.98 | 1.02 | 1.00 |
| 6 | 0.75 | 0.56 | 0.93 | 1.01 | 0.76 |
| 7 | 0.66 | 0.72 | 1.01 | 0.99 | 0.82 |
| 8 | 0.84 | 0.86 | 1.00 | 1.03 | 0.91 |
| 9 | 0.84 | 0.85 | 1.00 | 1.02 | 0.91 |
| 10 | 0.68 | 1.23 | 1.10 | 1.03 | 1.06 |
| 11 | 0.62 | 0.37 | 1.22 | 1.02 | 0.65 |
| 12 | 0.70 | 0.55 | 1.17 | 1.05 | 0.74 |
| 13 | 0.70 | 0.60 | 1.12 | 1.02 | 0.77 |
| 14 | 0.71 | 0.67 | 1.13 | 1.02 | 0.80 |
| 15 | 0.66 | 0.57 | 1.13 | 1.00 | 0.75 |
| 16 | 0.61 | 0.55 | 1.16 | 1.00 | 0.73 |

| Patient L – 6 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.01 | 0.90 | 1.05 | 1.03 | 0.96 |
| 3 | 1.00 | 0.70 | 1.24 | 1.03 | 0.86 |
| 4 | 0.99 | 0.62 | 1.06 | 1.02 | 0.82 |
| 5 | 0.96 | 1.03 | 1.14 | 1.03 | 1.01 |
| 6 | 0.86 | 0.56 | 1.27 | 1.00 | 0.77 |
| 7 | 0.73 | 0.72 | 0.98 | 1.00 | 0.83 |
| 8 | 0.90 | 0.86 | 1.01 | 1.03 | 0.92 |
| 9 | 0.82 | 0.84 | 1.03 | 1.01 | 0.90 |
| 10 | 0.78 | 1.41 | 1.18 | 1.05 | 1.16 |
| 11 | 0.72 | 0.40 | 1.32 | 1.04 | 0.68 |
| 12 | 0.71 | 0.59 | 1.18 | 1.03 | 0.76 |
| 13 | 0.71 | 0.66 | 1.17 | 1.03 | 0.79 |
| 14 | 0.71 | 0.66 | 1.17 | 1.03 | 0.79 |
| 15 | 0.68 | 0.61 | 1.13 | 1.00 | 0.77 |
| 16 | 0.67 | 0.54 | 1.10 | 1.02 | 0.73 |

| Patient M – 15 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 0.99 | 1.01 | 1.10 | 1.08 | 1.00 |
| 3 | 0.97 | 0.67 | 1.10 | 1.10 | 0.85 |
| 4 | 1.05 | 0.75 | 1.05 | 1.09 | 0.89 |
| 5 | 0.94 | 1.03 | 0.96 | 1.13 | 1.00 |
| 6 | 0.93 | 0.82 | 1.05 | 1.11 | 0.91 |
| 7 | 0.77 | 0.75 | 0.98 | 1.13 | 0.85 |
| 8 | 1.00 | 0.88 | 1.10 | 1.13 | 0.94 |
| 9 | 0.87 | 0.83 | 0.99 | 1.13 | 0.90 |
| 10 | 0.75 | 1.15 | 1.03 | 1.12 | 1.03 |
| 11 | 0.65 | 0.31 | 1.12 | 1.12 | 0.64 |
| 12 | 0.72 | 0.49 | 1.01 | 1.12 | 0.73 |
| 13 | 0.68 | 0.52 | 1.04 | 1.13 | 0.74 |
| 14 | 0.81 | 0.65 | 1.11 | 1.13 | 0.81 |
| 15 | 0.67 | 0.55 | 1.20 | 1.12 | 0.75 |
| 16 | 0.61 | 0.43 | 1.17 | 1.13 | 0.69 |

| Patient M – 6 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.14 | 1.00 | 1.08 | 1.10 | 1.02 |
| 3 | 1.15 | 0.74 | 1.10 | 1.13 | 0.91 |
| 4 | 1.25 | 0.77 | 1.13 | 1.07 | 0.94 |
| 5 | 1.10 | 1.11 | 1.02 | 1.12 | 1.07 |
| 6 | 1.13 | 0.95 | 1.08 | 1.10 | 1.00 |
| 7 | 0.90 | 0.77 | 0.94 | 1.12 | 0.88 |
| 8 | 1.11 | 0.92 | 1.04 | 1.11 | 0.98 |
| 9 | 1.04 | 0.88 | 0.96 | 1.11 | 0.95 |
| 10 | 0.81 | 1.38 | 1.13 | 1.12 | 1.14 |
| 11 | 0.84 | 0.39 | 1.05 | 1.12 | 0.70 |
| 12 | 0.74 | 0.56 | 1.12 | 1.13 | 0.76 |
| 13 | 0.81 | 0.65 | 1.12 | 1.13 | 0.81 |
| 14 | 0.81 | 0.65 | 1.12 | 1.13 | 0.81 |
| 15 | 0.78 | 0.60 | 1.02 | 1.13 | 0.79 |
| 16 | 0.83 | 0.61 | 1.00 | 1.12 | 0.80 |

| Patient N – 15 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 0.98 | 0.95 | 0.88 | 1.01 | 0.98 |
| 3 | 0.95 | 0.62 | 1.03 | 1.00 | 0.82 |
| 4 | 1.13 | 0.77 | 0.86 | 1.02 | 0.91 |
| 5 | 0.94 | 1.02 | 0.86 | 1.03 | 1.00 |
| 6 | 0.88 | 0.58 | 1.01 | 0.99 | 0.79 |
| 7 | 0.73 | 0.74 | 0.85 | 1.05 | 0.85 |
| 8 | 0.98 | 0.87 | 0.85 | 1.01 | 0.94 |
| 9 | 0.85 | 0.84 | 0.84 | 1.03 | 0.90 |
| 10 | 0.60 | 0.59 | 0.85 | 1.03 | 0.76 |
| 11 | 0.54 | 0.27 | 1.01 | 0.99 | 0.60 |
| 12 | 0.65 | 0.50 | 0.96 | 1.02 | 0.72 |
| 13 | 0.71 | 0.56 | 0.97 | 1.03 | 0.76 |
| 14 | 0.71 | 0.56 | 0.96 | 1.03 | 0.76 |
| 15 | 0.66 | 0.51 | 0.85 | 1.05 | 0.73 |
| 16 | 0.60 | 0.51 | 0.94 | 1.02 | 0.72 |

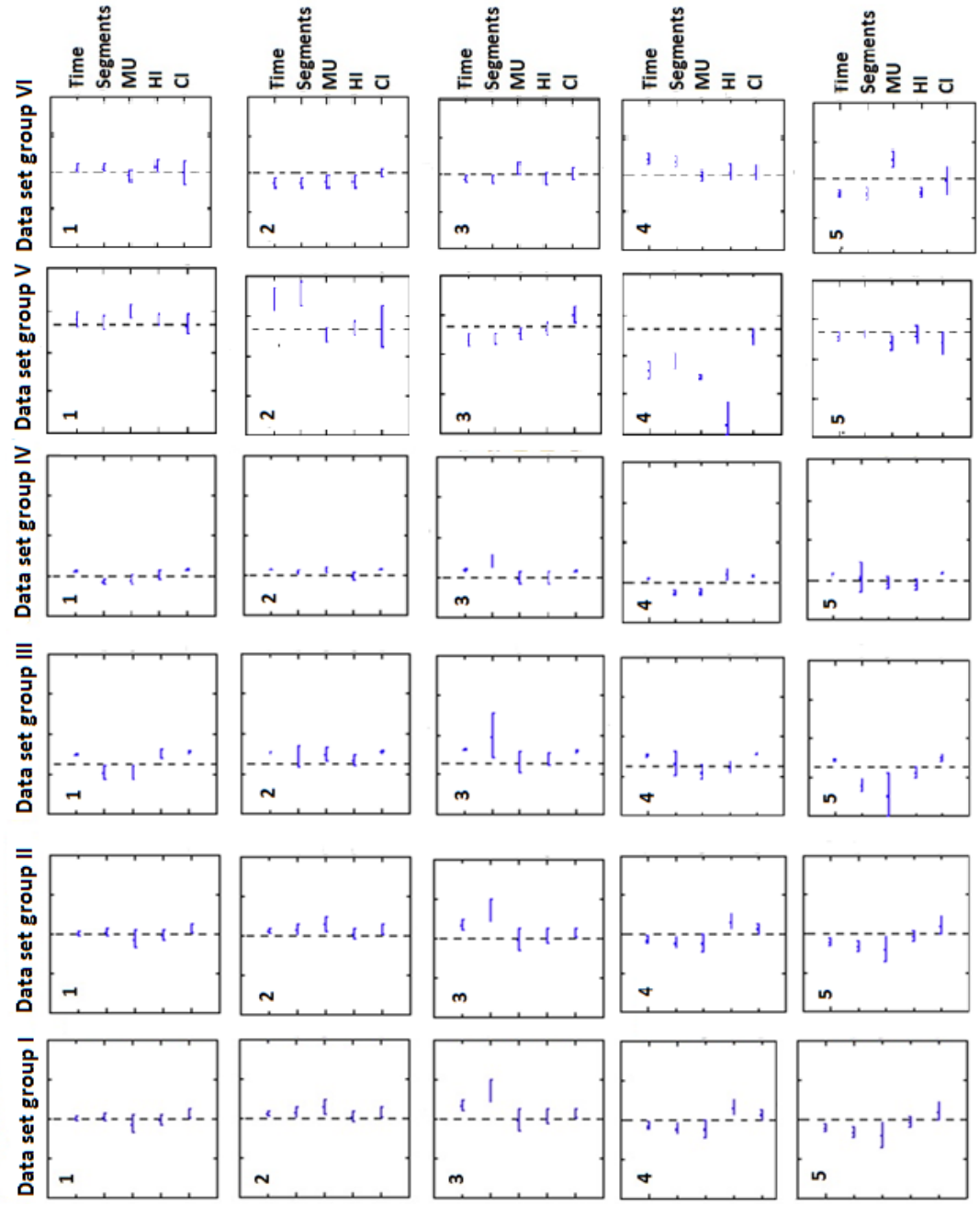
| Patient N – 6 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.07 | 0.91 | 0.83 | 1.04 | 0.97 |
| 3 | 1.05 | 0.66 | 0.88 | 1.05 | 0.86 |
| 4 | 1.20 | 0.74 | 0.88 | 1.00 | 0.92 |
| 5 | 1.06 | 1.12 | 0.81 | 1.05 | 1.06 |
| 6 | 0.98 | 0.71 | 0.90 | 1.02 | 0.87 |
| 7 | 0.83 | 0.78 | 0.82 | 1.07 | 0.88 |
| 8 | 1.08 | 0.88 | 0.87 | 1.04 | 0.96 |
| 9 | 0.97 | 0.80 | 0.85 | 1.04 | 0.91 |
| 10 | 0.70 | 0.71 | 0.81 | 1.07 | 0.82 |
| 11 | 0.75 | 0.40 | 1.03 | 1.03 | 0.69 |
| 12 | 0.71 | 0.57 | 0.87 | 1.06 | 0.76 |
| 13 | 0.79 | 0.64 | 0.77 | 1.07 | 0.81 |
| 14 | 0.79 | 0.64 | 0.77 | 1.07 | 0.81 |
| 15 | 0.70 | 0.58 | 0.88 | 1.06 | 0.77 |
| 16 | 0.67 | 0.48 | 0.80 | 1.08 | 0.72 |

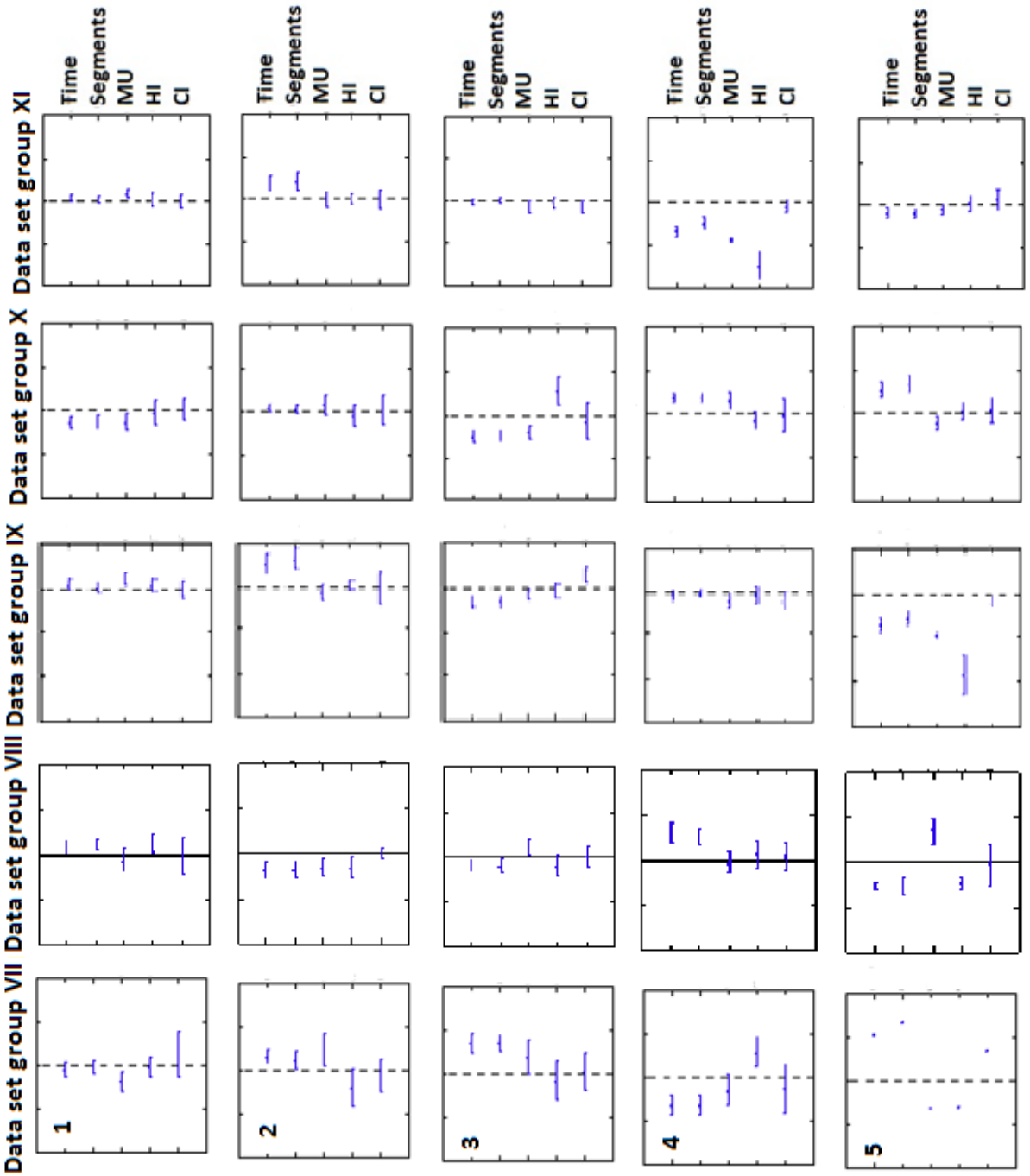
| Patient O – 15 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.04 | 1.02 | 1.37 | 1.04 | 1.02 |
| 3 | 1.03 | 0.80 | 1.04 | 1.04 | 0.92 |
| 4 | 1.09 | 0.76 | 1.18 | 1.05 | 0.91 |
| 5 | 1.02 | 1.20 | 1.18 | 1.03 | 1.09 |
| 6 | 0.96 | 0.82 | 0.46 | 1.06 | 0.91 |
| 7 | 0.92 | 0.95 | 1.06 | 1.02 | 0.97 |
| 8 | 1.09 | 1.02 | 1.04 | 1.05 | 1.03 |
| 9 | 0.98 | 0.96 | 1.21 | 1.05 | 0.98 |
| 10 | 0.84 | 1.54 | 1.41 | 1.02 | 1.21 |
| 11 | 0.70 | 0.39 | 1.24 | 0.91 | 0.68 |
| 12 | 0.77 | 0.62 | 1.23 | 0.97 | 0.80 |
| 13 | 0.78 | 0.62 | 1.23 | 0.96 | 0.80 |
| 14 | 0.78 | 0.62 | 1.19 | 0.96 | 0.80 |
| 15 | 0.83 | 0.73 | 1.26 | 1.00 | 0.85 |
| 16 | 0.77 | 0.66 | 1.00 | 1.00 | 0.81 |

| Patient O – 6 MV | | | | | |
|---|---|---|---|---|---|
| **Plan No.** | **Total MU's** | **Total Segments** | **HI** | **CI** | **Time delivery (s)** |
| 1 | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| 2 | 1.09 | 0.96 | 1.31 | 1.02 | 1.00 |
| 3 | 1.09 | 0.81 | 1.08 | 1.01 | 0.93 |
| 4 | 1.18 | 0.76 | 1.06 | 1.03 | 0.92 |
| 5 | 1.05 | 1.22 | 1.03 | 1.07 | 1.11 |
| 6 | 1.05 | 0.87 | 0.95 | 1.03 | 0.95 |
| 7 | 0.97 | 0.93 | 1.05 | 1.00 | 0.96 |
| 8 | 1.21 | 1.04 | 1.01 | 1.06 | 1.05 |
| 9 | 1.07 | 0.96 | 1.15 | 1.03 | 1.00 |
| 10 | 0.84 | 1.58 | 1.43 | 1.03 | 1.23 |
| 11 | 0.72 | 0.41 | 1.41 | 1.01 | 0.69 |
| 12 | 0.78 | 0.69 | 1.22 | 1.01 | 0.83 |
| 13 | 0.85 | 0.78 | 1.22 | 1.00 | 0.88 |
| 14 | 0.85 | 0.78 | 1.22 | 1.00 | 0.88 |
| 15 | 0.79 | 0.74 | 1.25 | 0.98 | 0.85 |
| 16 | 0.79 | 0.68 | 1.25 | 1.04 | 0.83 |

## 9.5 Appendix E

### 9.5.1 Cluster profiles for all data set groups




Data set group VII
Data set group VIII
Data set group IX
Data set group X
Data set group XI
Time
Segments
MU
HI
CI
1
2
3
4
5

## 9.6 Appendix F

### 9.6.1 **MapCHECK measurements**

*Table 9.2: Percentage pass rate results of the three measurements on the linac for Patient Y*

| **Patient Y** | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | **Measurement 1** | | | |
| **Plan No.** | Field 1 | Field 2 | Field 3 | Field 4 | Field 5 | Field 6 | Field 7 |
| **Default** | 88.2 | 93.1 | 87.4 | 85.8 | 92.0 | 85.4 | 92.3 |
| **3** | 90.8 | 91.7 | 90.3 | 86.5 | 91.7 | 86.2 | 89.0 |
| **6** | 91.8 | 92.6 | 93.5 | 90.4 | 91.9 | 90.2 | 91.3 |
| **7** | 96.9 | 97.4 | 95.1 | 95.0 | 97.0 | 94.4 | 92.9 |
| **9** | 91.1 | 94.4 | 94.0 | 92.6 | 95.7 | 89.8 | 95.3 |
| **11** | 95.6 | 93.1 | 97.8 | 84.6 | 90.5 | 95.3 | 95.9 |
| **12** | 92.8 | 92.7 | 87.6 | 90.1 | 95.8 | 92.0 | 94.3 |
| **13** | 93.1 | 91.5 | 90.3 | 87.2 | 96.4 | 92.8 | 95.2 |
| **14** | 94.7 | 91.0 | 90.7 | 90.7 | 94.9 | 92.0 | 95.2 |
| **15** | 93.9 | 96.3 | 87.9 | 92.2 | 94.4 | 91.4 | 92.6 |
| **16** | 91.5 | 90.7 | 90.7 | 89.7 | 88.7 | 91.3 | 89.7 |
| | | | | **Measurement 2** | | | |
| **Plan No.** | Field 1 | Field 2 | Field 3 | Field 4 | Field 5 | Field 6 | Field 7 |
| **Default** | 92.8 | 93.2 | 92.4 | 88.3 | 94.0 | 88.8 | 89.6 |
| **3** | 95.2 | 93.2 | 92.4 | 87.4 | 90.2 | 86.2 | 85.9 |
| **6** | 95.0 | 93.8 | 93.1 | 89.3 | 94.1 | 89.8 | 87.9 |
| **7** | 97.8 | 94.1 | 91.9 | 95.3 | 94.4 | 91.2 | 92.3 |
| **9** | 92.0 | 94.7 | 96.2 | 93.3 | 94.4 | 91.0 | 94.1 |
| **11** | 96.2 | 95.1 | 99.1 | 86.1 | 93.1 | 97.0 | 95.9 |
| **12** | 95.6 | 93.2 | 94.3 | 90.1 | 94.2 | 91.6 | 92.8 |
| **13** | 95.9 | 88.7 | 96.2 | 90.7 | 97.6 | 93.1 | 96.3 |
| **14** | 96.6 | 89.9 | 95.0 | 93.3 | 95.2 | 91.9 | 94 |
| **15** | 95.7 | 94.9 | 90.7 | 92.4 | 91.9 | 94.3 | 93.4 |
| **16** | 96.0 | 94.3 | 93.5 | 90.9 | 91.6 | 94.6 | 93.2 |
| | | | | **Measurement 3** | | | |
| **Plan No.** | Field 1 | Field 2 | Field 3 | Field 4 | Field 5 | Field 6 | Field 7 |
| **Default** | 92.8 | 92.9 | 94.6 | 88.3 | 95.2 | 88.2 | 91.9 |
| **3** | 95.7 | 93.8 | 94.0 | 88.0 | 92.7 | 88.4 | 90.5 |
| **6** | 96.0 | 96.4 | 95.5 | 91.6 | 95.1 | 89.9 | 90.5 |
| **7** | 98.8 | 97.2 | 95.3 | 97.1 | 97.0 | 91.8 | 94.6 |
| **9** | 94.0 | 96.7 | 94.5 | 94.1 | 95.6 | 91.3 | 95.5 |
| **11** | 96.5 | 93.9 | 98.4 | 87.7 | 92.8 | 97.6 | 96.5 |
| **12** | 95.9 | 93.8 | 93.0 | 90.1 | 94.2 | 92.5 | 95.1 |
| **13** | 95.6 | 92.1 | 94.0 | 89.5 | 97.3 | 92.8 | 96.8 |
| **14** | 95.9 | 89.8 | 95.3 | 93.3 | 95.2 | 92.8 | 94.0 |
| **15** | 95.4 | 96.9 | 86.4 | 93.9 | 96.7 | 91.3 | 89.7 |
| **16** | 96.0 | 91.0 | 88.4 | 91.8 | 88.4 | 90.4 | 88.8 |

*Table 9.3: Percentage pass rate results of the three measurements on the linac for Patient AA*

| Patient AA | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Measurement 1** | | | | | | | |
| **Plan No.** | Field 1 | Field 2 | Field 3 | Field 4 | Field 5 | Field 6 | Field 7 |
| **Default** | 88.2 | 93.1 | 87.4 | 85.8 | 92.0 | 85.4 | 92.3 |
| **3** | 90.8 | 91.7 | 90.3 | 86.5 | 91.7 | 86.2 | 89.0 |
| **6** | 91.8 | 92.6 | 93.5 | 90.4 | 91.9 | 90.2 | 91.3 |
| **7** | 96.9 | 97.4 | 95.1 | 95.0 | 97.0 | 94.4 | 92.9 |
| **9** | 91.1 | 94.4 | 94.0 | 92.6 | 95.7 | 89.8 | 95.3 |
| **11** | 95.6 | 93.1 | 97.8 | 84.6 | 90.5 | 95.3 | 95.9 |
| **12** | 92.8 | 92.7 | 87.6 | 90.1 | 95.8 | 92.0 | 94.3 |
| **13** | 93.1 | 91.5 | 90.3 | 87.2 | 96.4 | 92.8 | 95.2 |
| **14** | 94.7 | 91.0 | 90.7 | 90.7 | 94.9 | 92.0 | 95.2 |
| **15** | 93.9 | 96.3 | 87.9 | 92.2 | 94.4 | 91.4 | 92.6 |
| **16** | 91.5 | 90.7 | 90.7 | 89.7 | 88.7 | 91.3 | 89.7 |
| **Measurement 2** | | | | | | | |
| **Plan No.** | Field 1 | Field 2 | Field 3 | Field 4 | Field 5 | Field 6 | Field 7 |
| **Default** | 92.8 | 93.2 | 92.4 | 88.3 | 94.0 | 88.8 | 89.6 |
| **3** | 95.2 | 93.2 | 92.4 | 87.4 | 90.2 | 86.2 | 85.9 |
| **6** | 95.0 | 93.8 | 93.1 | 89.3 | 94.1 | 89.8 | 87.9 |
| **7** | 97.8 | 94.1 | 91.9 | 95.3 | 94.4 | 91.2 | 92.3 |
| **9** | 92.0 | 94.7 | 96.2 | 93.3 | 94.4 | 91.0 | 94.1 |
| **11** | 96.2 | 95.1 | 99.1 | 86.1 | 93.1 | 97.0 | 95.9 |
| **12** | 95.6 | 93.2 | 94.3 | 90.1 | 94.2 | 91.6 | 92.8 |
| **13** | 95.9 | 88.7 | 96.2 | 90.7 | 97.6 | 93.1 | 96.3 |
| **14** | 96.6 | 89.9 | 95.0 | 93.3 | 95.2 | 91.9 | 94 |
| **15** | 95.7 | 94.9 | 90.7 | 92.4 | 91.9 | 94.3 | 93.4 |
| **16** | 96.0 | 94.3 | 93.5 | 90.9 | 91.6 | 94.6 | 93.2 |
| **Measurement 3** | | | | | | | |
| **Plan No.** | Field 1 | Field 2 | Field 3 | Field 4 | Field 5 | Field 6 | Field 7 |
| **Default** | 92.8 | 92.9 | 94.6 | 88.3 | 95.2 | 88.2 | 91.9 |
| **3** | 95.7 | 93.8 | 94.0 | 88.0 | 92.7 | 88.4 | 90.5 |
| **6** | 96.0 | 96.4 | 95.5 | 91.6 | 95.1 | 89.9 | 90.5 |
| **7** | 98.8 | 97.2 | 95.3 | 97.1 | 97.0 | 91.8 | 94.6 |
| **9** | 94.0 | 96.7 | 94.5 | 94.1 | 95.6 | 91.3 | 95.5 |
| **11** | 96.5 | 93.9 | 98.4 | 87.7 | 92.8 | 97.6 | 96.5 |
| **12** | 95.9 | 93.8 | 93.0 | 90.1 | 94.2 | 92.5 | 95.1 |
| **13** | 95.6 | 92.1 | 94.0 | 89.5 | 97.3 | 92.8 | 96.8 |
| **14** | 95.9 | 89.8 | 95.3 | 93.3 | 95.2 | 92.8 | 94.0 |
| **15** | 95.4 | 96.9 | 86.4 | 93.9 | 96.7 | 91.3 | 89.7 |
| **16** | 96.0 | 91.0 | 88.4 | 91.8 | 88.4 | 90.4 | 88.8 |

## 9.7 Appendix G

### 9.7.1 Ethics approval

UNIVERSITY OF THE FREE STATE
UNIVERSITEIT VAN DIE VRYSTAAT
YUNIVESITHI YA FREISTATA
UFS UV

Research Division
Internal Post Box G40
☎(051) 4052812
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Ms H Strauss

E-mail address: StraussHS@ufs.ac.za

2014-07-30

REC Reference nr 230408-011
IRB nr 00006240

MS NS FOURIE
C/O PROF W RAE
DEPT OF MEDICAL PHYSICS
FACULTY OF HEALTH SCIENCES
UFS

Dear Ms Fourie

ECUFS NR 109/2014
MS NS FOURIE DEPT EQURA HEALTH, CAPE TOWN
PROJECT TITLE: OPTIMISATION OF DELIVERY EFFICIENCY IN PROSTATE INTENSITY MODULATED RADIOTHERAPY PLANNING

1. You are hereby kindly informed that the study was approved at the Ethics Committee meeting held on 22 July 2014.
2. Committee guidance documents: Declaration of Helsinki, ICH, GCP and MRC Guidelines on Bio Medical Research. Clinical Trial Guidelines 2000 Department of Health RSA; Ethics in Health Research: Principles Structure and Processes Department of Health RSA 2004; Guidelines for Good Practice in the Conduct of Clinical Trials with Human Participants in South Africa, Second Edition (2006); the Constitution of the Ethics Committee of the Faculty of Health Sciences and the Guidelines of the SA Medicines Control Council as well as Laws and Regulations with regard to the Control of Medicines.
3. Any amendment, extension or other modifications to the protocol must be submitted to the Ethics Committee for approval.
4. The Committee must be informed of any serious adverse event and/or termination of the study.
5. All relevant documents e.g. signed permission letters from the authorities, institutions, changes to the protocol, questionnaires etc. have to be submitted to the Ethics Committee before the study may be conducted (if applicable).
6. A progress report should be submitted within one year of approval of long term studies and a final report at completion of both short term and long term studies.

7. Kindly refer to the ETOVS/ECUFS reference number in correspondence to the Ethics Committee secretariat.

Yours faithfully

.....

**PROF WH KRUGER**
**CHAIR: ETHICS COMMITTEE**

Cc Prof W Rae

## 9.7.2 **Permission letter**

EQURA HEALTH
*PO Box 15811, Panorama, 7506*
**T:** *021-914-3600* **F:** *021-949-4112*

TO WHOM IT MAY CONCERN

**PERMISSION TO USE EQURA HEALTH EQUIPMENT IN THE COURSE OF STUDY**

It is hereby stated that

Student: Nicola Fourie; 8208080062087

An Equra Health employee, has been given permission to use Equra Health equipment in the course of study towards her M.Med.Sc. degree with the title:

"Optimisation of Deliverability when Planning Prostate Intensity Modulated Radiation Therapy"

Yours sincerely

**ERHARDT KORF**
**CHIEF OPERATING OFFICER**

19 MAY 2014

## 9.8 Appendix H

### 9.8.1 **Abstracts of presentations presented at the SAAPMB Congress 2015.**

These two abstracts were also published in the European Journal of Medical Physics, 2015, Volume 31, pages S4-5

# DERIVING A TIME DELIVERY MODEL FOR A SIEMENS ARTISTE™ LINAC

Fourie, NS[a], Ali, OA[ab], Rae, WID[b]

[a]*Department of Medical Physics, Equra Health*

[b]*Department of Medical Physics, University of the Free State*

**Introduction:** With IMRT delivery time is significantly longer than with 3DCRT; therefore accurate dose delivery becomes difficult due to intra-fractional patient movement. To our knowledge there is as yet no time delivery model proposed for a Siemens® ARTISTE™ Linear Accelerator (Linac). Our aim is to propose such a model.

**Materials and methods:** Using the principles of the time delivery model created by Li and Xing for a Varian Linac (Med Phys. 2011; 38(9):4912–9), a formula was proposed that determines time delivery on a Siemens® ARTISTE™ Linac. We added the Radio Frequency (RF) wave component to our model because wave frequency warm up time is significant for a Siemens Linac. Machine input parameters such as gantry speed, MLC speed and delay and RF wave time were confirmed using a WIN (Sports timer) stop watch. We tested our derived model by selecting ten random prostate IMRT plans from our clinic. These treatment plans were delivered on the Linac and measured.

**Results:** The delivery time measured was between 314s and 480s. The largest percentage difference, between measured and calculated was 3.9% (13s) and the smallest 0.2% (1s). The average percentage difference was 1.78%. These results correlated well with published reports. These differences seem to be insignificant, 99% CI [408; 400].

**Conclusion:** Deriving a time delivery model makes it possible to estimate the time delivery before dose delivery is done on a Linac. This is important since we can choose a plan, from a pool of clinically acceptable plans, with the shortest delivery time, and thus increase dose delivery accuracy by minimizing patient movement.

**Keywords:** Time delivery model, IMRT.

# OPTIMISATION OF PROSTATE INTENSITY MODULATED RADIATION THERAPY WHEN USING AN XiO TPS

Fourie, NS[a], Ali, OA[ab], Rae, WID[b]

[a]*Department of Medical Physics, Equra Health*

[b]*Department of Medical Physics, University of the Free State*

**Introduction:** Growing evidence supports conformal target dose escalation for prostate cancer treatment and this is achievable using IMRT. More Monitor Units (MU's) and segments improve conformity but extend delivery times, thus decreasing dose delivery accuracy. Literature shows secondary induced cancer incidence is proportional to beam-on time (MU). IMRT delivery efficiency can be achieved by changing optimization parameters within the treatment planning system (TPS). Our aim is to recommend optimization parameters to improve delivery efficiency for prostate IMRT treatments while maintaining plan quality.

**Materials and methods:** The CMS XiO TPS version 4.80 was used to re-optimize 15 already treated clinical prostate IMRT plans to determine dependence of total MU and segment number on optimization parameters. Both segmentation methods; Sliding Window (SLW) and Synchronized Moving Aperture Radiation Therapy (SMART) sequencing, were used. The optimization parameters for SLW were: minimum MU per segment (MMUS), Intensity levels (IL's), minimum segment size (MSS), general high filter (GH) and intermediate low (IntLow) and high (IntHigh) filters. For SMART segmentation parameters were: MMUS, minimum segment area (MSA), suppression factor (SSF) and simple low (SL) and high (SH) filters. The outcome was assessed using k-means clustering for 5 variables, total MU's, segments, homogeneity (HI), conformity index (CI), and delivery time

**Results:** MMUS, MSS and MSA had most influence on total MU's and segments, generating maximum differences of 20% and 40% for SLW and SMART methods respectively.

Total segments influenced delivery time most, thus the inter-segmental time (MLC speed) is more penalising than the intra-segmental time (MU's delivered).

**Conclusion:** Changing optimization parameters during IMRT planning can improve IMRT delivery efficiency to the prostate.

**Keywords:** Optimisation, IMRT